HANDBOOK OF TROPICAL DERMATOLOGY AND MEDICAL MYCOLOGY

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edited by

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Amsterdam

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VOLUME I



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PREFACE

This work was conceived and born in a P.O.W. camp somewhere in the Pacific. It was first published in a more condensed form in the Dutch language, after which some eighty authors with experience of dermatology in the tropics cast it in its present mould. The task of editing the work was far from easy but it was a pleasant one. I wish here to express my sincere thanks to all contributors, and to add a word of praise for those who collaborated in the work of translation from different languages into homogeneous English my ex-fellow P.O.W. J. RINTOUL (London) SIR HAROLD H. SCOTT (Braintree, Essex) Dr S. T. ANNING (Leeds) Mr E. VAN LOO (Leyden), Dr W. MULHALL CORBET (Amsterdam) and Dr E. LIPMAN COHEN (London)

The selection of authors and other co-workers does not in the least imply that other prominent specialists have been ignored On the contrary we are well aware that the work lacks the names of some experienced authors. Among those represented in the work the reader will find the names of some who are not dermatologists for the skin specialist may obtain considerable assistance from the investigations and conclusions of workers in other branches of medicine. Although typographical uniformity has been aimed at as far as was feasible, it was not possible to keep the subdivision of the chapters the same in all cases

Photographs showing no source of origin were supplied by the authors of the chapters concerned. Only about five illustrations have been duplicated in overlapping descriptions.

We sincerely hope that the work of our team ranging as it does along the whole equator may render good service, alike to dermatologists and physicians in all parts of the tropics.

Amsterdam, June 1952 SIMONS

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CHAPTER 1

GENERAL SURVEY

R. D. G. PH. SIMONS

Amsterdam

A. INTRODUCTION TO THE HISTORY AND DEVELOPMENT OF TROPICAL DERMATOLOGY

Not until the nineteenth century did dermatology in the tropics develop on scientific lines, parallel with tropical medicine, after centuries of idol-worship based on superstition, fear and pseudo-scientific notions about heredity, food poisoning and divine punishment. Missionary and military doctors, as a rule, were the first to make a study of the diseases in question but owing to the slow and inefficient postal communications in those early days there were unduly long delays in the mutual exchange of views and experiences. One result of this is that the majority of the diseases have come to our knowledge under a large number of synonyms which, because of the varying descriptions, were originally regarded as the names of separate diseases *suorum generum*. Since scientific knowledge thus made its escape by such devious and difficult routes it was often thought that the diseases which, with the aid of this knowledge, were also observed elsewhere, had in fact, spread along this same route, whereas, in many cases, it was not the disease but the observation and knowledge of it that had spread.[1]

[1] An interesting example of this is the name *sika* (chigger) for the *Sarcopsylla* (or *Tunga*) *penetrans*. *Sika* is an American-Indian word; that this disease is also called *chique* in Senegal (W. Africa) is due to the fact that the affection was discovered there when it was already known under the name of "sika" in the French colonies in America. We have here an American-Indian name current in Africa—to set off the many African (slave) names in America, *e.g.* *bubu*, *buasi* etc.

Obviously a great many diseases were observed before ever being described but old descriptions like tradition, usually provide a merely historical and sometimes an epidemiological insight which, too may not be correct because owing to the faulty diagnostics of antiquity and the dark ages many different diseases—this in contrast to the above mentioned avalanche of synonyms—were grouped together under a single name.

We need only think of *variola* by which either papules (varus) and pustules or "polymorphism" (varus variegatus) were denoted of *leprosy* which included diverse squamous macular and ulcerative dermatoses and *pestis* (*cf* pestilence plague) to which different fatal diseases were ascribed, even if the addition of some adjective was needed to indicate a special form of the genus.

A backward look at medical history prior to 1800 therefore, would yield, instead of a picture of scientific development, rarely more than a jumble of diseases usually very badly described but none the less highly important for the study of the cultural development of countries and peoples In this, however we must take into account the extremely strange theories prevalent at the time, in view of the many rites and customs which were based not on science but on the art of healing (better the fear of illness") of those days.

Temples, churches, altars and totem-poles arose when disease and distress increased, and sometimes they were as readily demolished if they failed to come up to what was expected of them. The Mosaic ritual laws relating to hygiene, which Moses in his turn, had learned at the Egyptian court (they are also found in the papyrus of EBERS) purported to serve, among other things, as prophylaxis against leprosy in man and the risk of contracting it from his clothes or residence[1] The totem-pole of the Red Indians was often no more than the god of disease, and the tattooed masks of the Negroes and many Asiatic tribes aimed at frightening away the spirits of disease or to make one self unrecognizable by them[2] Special *diets* such as adopted by Negro slaves from their Jewish masters and combined with their African

[1] Ritual circumcision was not intended as a hygienic measure but as a sacrifice (*vide* Gen. 17 12 Le n. 12 3 Deut 30 6 Jer 4 4 Sam. 1–18 25)

[2] Just as the face was altered by such a mask it was (and still is) also attempted to mislead the spirits by changing the name of the patient a trick which has caused epidemiological investigators no end of trouble, about which more anon.

fetishism as *terrifa faith* *rites* like self flagellation or fakir's performances, and *traditions* such as the Oberammergau passion plays (which evolved as a result of a vow made when the city was threatened by



1 Indonesian mask with corymbiform grouping of umbilicated papules and tubers, saddle nose and facial paralysis.

plague) all these pseudo-prophylactics stem from a civilization affected by disease.

It was not in the tropics that Europeans first made the acquaintance of tropical diseases. Did not the Oracle foretell the coming of the Dorian war and of a great plague? About 500 B C. the plague ravaged Athens, which meant the loss of its great ruler PERICLES and the end

of its golden age[1] A thousand years later a new epidemic came from Egypt and swept the Roman empire. Under the name of the "Black Death the disease, in the fourteenth century spread all over Europe depopulating many towns One of the crusades never reached the Holy City owing to the annihilation of the troops by bubonic plague (Scott). In the fifteenth century—and probably before that—Europe, while still suffering from the effects of the Black Death, was visited by an epidemic of smallpox by which name, however not only variola was meant for the "Spanish pox" (probably imported from South America) is generally assumed to have actually been *morbus gallicus i.e.* syphilis Again, under the name of *morbus hungaricus typhus* came over from Asia Minor and decimated the army of Maximilian II (Typhus was also a great scourge among Napoleon s troops in Russia[2]) Typhus was not however limited to Asia Minor its sister disease, *tabardillo* which raged in Mexico at the time of the Aztecs, was also a rickettsiosis while another rickettsiosis *tsutsugamushi* disease has been prevalent in Japan.

Nor was leprosy unknown in Europe although it is practically certain that the name was used to cover a large number of diseases which, according to modern notions are not genuine leprosy but either vitiligo psoriasis or one of many other dermatoses. The word "lepra which actually means scaly is really a bad translation of the biblical term tsarat" or "zarath meaning struck by God" It is used in the Bible side by side with pestilence" and fiery serpents" and it is far from improbable that the three terms were used to denote many different epidemic diseases (In fact, an end came to the epidemic of leprosy after various so-called "leprosies began to be differentiated and the term *morbus gallicus* came into vogue.)

The fifth plague of Egypt was pestilence among the cattle, and the sixth was characterized by sores and ulcers in both man and animals (? leishmaniasis) The Book of Leviticus mentions leprosy According to Numbers (21) many men were "bitten by fiery serpents" and according to Samuel II seventy thousand men died of pestilence

[1] Allen Pusey *History of Dermatology* Springfield Ill also Ralph Major *Disease and Destiny* (1937) Richter, *Handbuch für Haut und Geschlechtskrankheiten* XII–2/XV–1 and H Harold Scott *A History of Tropical Medicine* London 1939

[2] Plague decimated his army in Egypt.

Whether the fiery snakes that plagued the Jews in Edom on the Red Sea were real snakes or maybe, medina worms (*Dracunculus*[1] *medinensis*) and whether the serpent which Moses had fixed on his staff was



2. MEDINA WORM the "fiery snake" that plagued the Jews on the Red Sea, the origin of Moses' staff and Aesculapius attribute.

(Bairnsw-Roussel Katzenellenbogen Simons)

also a medina worm which Aesculapius later adopted as his emblem is, se non é vero" at any rate "bene trovato"

Under which of the names mentioned above, or their equivalents should one place, historically such diseases as *scabies impetigo eczema* or *anthrax* (of which AVICENNA of Bagdad gave a clear description as

= serpent (Gr). This disease is, in fact, of frequent occurrence on the shores of the Red Sea. The name *aska* (= worm cf also *ascaris* = roundworm) + *hpds* (to sense) as the origin of the name *asklepios* (Aesculapius) strongly supports this assumption. The cup of water carried by Aesculapius da ghter Hygiea, and which the medina worm is seen to approach, also becomes explicable in the same connection. (See Fig 3) (See also REINER MULLER, DER UMSCHAU 1950)

early as 1000 A.D.)? The disease of Job was scabies—or maybe leishmaniasis or furunculosis—rather than leprosy and the sores of Lazarus which were licked by the dogs (quite a customary treatment in those days for that matter) and from which the terms "mal lazare" and "lazaret(to)" are derived, may have been what is now called—and even then faultily—"desert sores".

Penetrating further in the direction of the equator, we shall find that there, also different skin diseases were grouped together under one and the same name, although there are certain cases, for instance, of leprosy which, however clearly recognizable they appear are still held in doubt by some. Thus in Angkor (Cambodia) the monument of "Le Roi Lépreux" shows the leprous king with mutilated hands. JEANSELME, however doubted the diagnosis and contested the king's right to the epithet, on the ground that not leprosy but the wear and tear of time had caused the deformities. On the other hand the fact remains that the statue is probably that of the God of Death DHARMARAJA instead of JAYAVARMAN VII who was called the leprous king but of whom no statue is known, thus leaving the diagnosis open to question.

In India various skin diseases were held to be epidemics sent by God, and even today leprosy is regarded, in several parts of Asia (*e.g.*, Bali) as a divine punishment with which man ought not to interfere and which, therefore, must not be treated.

Some diseases were named after enemy peoples. The most telling example of this is surely that ubiquitous complaint, syphilis: "Franzosenkrankheit", "Christian's disease" (among the Turks), "Spanish pox" (among the Dutch), "mal Espagnol" (among the Portuguese), "mal napolitain" (in France) etc. Yaws is called in Ceylon "parangi" after the "white interlopers". In Surinam the flea is called *chiereste*, the bed-bug *duistre* (*i.e.* German) and the Trombicula batatas "*patatta lossa*"—not after the batatas-plant, but after the nickname "patatta" given to the Dutch. (See page 142).

Among the skin diseases which have always caused a good deal of confusion (and still do!), we may mention, apart from leprosy and smallpox, syphilis, leishmaniasis and yaws.

Framboesia or *yaws* was described by JACOBUS BONTIUS in Indonesia as early as 1642. He, however, called it "Ambonese pox" because he was struck by a certain resemblance between this disease and Spanish

pox" At about the same time Piso described what he called "bouba" in South America. By this term he clearly meant yaws but the word "bouba" is still being used today for cutaneous leishmaniasis which was described by Russell under the name of *aleppo boil* as early as 1756,



3 Lazarus as described in the New Testament parable, suffering from ulcers, which were licked by dogs. However this was not intended as proof of a distressful condition, because the licking of wounds by dogs was a customary treatment in ancient times.

(After a drawing by Glaymer Amsterdam)

and owes its official name to Leishman who in 1903 discovered its transmitting agent in a case of kala-azar

Gangosa (literally "muffled voice") first described by Bajou in 1773 and called *rhinopharyngitis mutilans* by Leys in 1906 appeared to be closely akin to yaws In contradistinction to *rhinoscleroma* which disease may be recognized from the nose of Butu Terong one of the figures in the Indonesian wayang plays[1] Rhinoscleroma is caused by a bacillus which is probably identical with that of *granuloma venereum*

[1] Steenman, *Cibatijdschrift* (*Ciba journal*), 1949

(SNIJDERS). FOSTER JOHNS[1] in fact quite rightly described at Jamaica a case of granuloma venereum of the nose (1924), an illustration of which is given later on.

While on the subject of noses we may remind the reader of the *goundou* of the "horny man" discovered by MACALISTER in West Africa (1882). This affection—with its positive Wassermann reaction—is also known by the name of "gros nez". *Goundou* itself actually means nothing more than "bump". The word is current in Surinam, where any bump, whether a bony exotosis or an excrescence on a plant, is called a "kunduh". Kunduh may also be a sebaceous cyst or a lipoma, but the *goundou disease* is either periostitis ossificans or ostitis fibrosa. Whether the goundou disease occurred in South America prior to the period of slavery is not certain, despite one or two findings (*e.g.* by LITTLE). In any case the abnormal noses on the pictures decorating ancient pots of the Inca Indians were no "kunduh" cases, but very probably meant to represent the symptoms of *espundia* or American leishmaniasis.

Having now arrived, via gangosa and rhinoscleroma in Asia, at goundou in Africa and kunduh in South America, we may consider for a moment two other notions which—as has happened so often in tropical medicine—crossed the ocean in a similar manner. The first is "*boassi*" by which is meant, in Surinam, leprosy. The name, however, is derived from the boassi worm which, in its turn, is named after the village of Boassi on the Gold Coast. The second is "*bobo*", derived from the African Kwa word for "bogey man" or the African Ewe word for "swollen"; it is at present current in Surinam to denote *filariasis Bancrofti* with its characteristic elephantiasic legs.

And so the farrago of pox, pestilences, leprosies[2] and syphilis, all of which meant little more than "skin disease" less than a century ago—the whole of this medley of diseases was so to speak spread all over the globe by explorers, soldiers, crusaders and slaves.

In Europe large numbers of sufferers from skin diseases were formerly locked up to prevent the disease from spreading, in so-called leprosaria—gruesome precursors of the modern dermatological

[1] International Congress on Health Problems, Jamaica, 1924.

[2] The Arabs, who in the same breath, referred to both lepra-blood and the menses as "poison", knew 18 different "leprosies".

clinics (in the 17th century there were 19 000 leprosaria in Europe, *cf* LÖWE)—because even the sight of these unclean ones was feared as if it were the scourge of Medusa and in the tropics—horribile dictu—this method is, in some cases being applied even today We are also reminded in this connection of PIZARRO who caused all



4 The false "Roi lépreux" since this is the weathered statue of the God DHARMARAJA and not of JAYAVARMAN, who was called the leprous king but of whom no statue is known.

(Musée de l'Homme – Paris)

sufferers from *pinta* (spotted sickness) to be isolated under the diagnosis leprosy and of the Japanese who as late as 1942, drowned every one of the lepers in the island of Nauru It might also be interesting to know the number of benign cases which are still being kept isolated to day in the company of malignant ones.

However to deal in detail with all the historical facts would mean writing a book on the history of tropical medicine, and divert us from our purpose of giving only a brief introduction to its historical

development the more so since this aspect will also be touched upon in most of the following chapters

B. THE TERMINOLOGICAL JUNGLE OF TROPICAL DERMATOLOGY

Rather let us try to disentangle our forefathers linguistic heritage, and examine systematically the babel of tongues in tropical dermatology with its many double names such as puru puru, lambo lambo loa loa, craw craw and bubu—at any rate in so far as there can be any question of a system in such an attempt.

For it must not be thought that all sores itches, pox and "boutons" are synonyms. Even some practically specific names have been cor rupted into names of other diseases altogether Thus, *yaws* is the English (derived from the African), and *pian* the French name[1] for framboesia tropica" but *bush yaws* and *pian bois* are synonyms of *espundia* which, as mentioned above, denotes American leishmaniasis. *Pian dartre* however in its turn, is annular[2] yaws (often confused with annular syphilis) also known as *ringworm yaws* but *dartre volante* is circumscribed pityriasis capitis, while *ringworm* without the suffix yaws" means tinea of the body beard or scalp

Again, *crab yaws* is the form of secondary yaws which affects the patient's soles and causes him to walk like a crab In Indonesia it is also known by the name of *bubul* but *buboh* is the vernacular term for widespread yaws as well as for leishmaniasis Another name for crab yaws is *durian rare* after the South Asiatic fruit (Durio zibethinus) which is so famous for its taste and so notorious for its stench.

The latest is *pintoid yaws* of which we do not yet know for certain whether it is pinta or yaws or maybe a combination of these two diseases[3] A similar case is that of *bejel* which is alternatively regarded as a form of yaws or as non venereal syphilis The treponematoses syphilis, yaws and pinta, with all their more or less well-known sub-

[1] Derived from the American-Indian.

[2] The difference between *annular* and *circinate* is often held to be that the former denotes a closed circle and the latter a fragment of circle Semantically however, "annular is not circular but ring-shaped and only applicable in that sense to affections *surrounding* or enclosing something (*e.g.*, a wrist or a finger).

[3] Pintoid yaws should not be confused with *circinate achromia* which is also seen in psoriasis, tinea versicolor etc.

types such as bejel *frengi* (genital primary syphilis in Syria) and the non-tabetic, non-paralytic *syphilis africanum et asiaticum* are caused by organisms which cannot be distinguished from one another by hitherto available methods. It may be suspected that these diseases are caused by the same spirochaeta which, all according to the particular syndrome it arouses is transmitted either directly or through an intermediary host (Hippelates?) after having lost certain properties in the process[1]

Does this seem a strange suggestion? What, then, do we see in the



5 Buru terong, one of the figures of the Indonesian wayang plays with rhinoscleroma.

case of leishmaniasis particularly in kala-azar, where the parasite disguises itself in the sandfly as leptomonas loses its flagellum in the human body and appears in the guise of a Leishman Donovan body? And what about Oroya fever and verruga peruviana which, despite a great deal of contradiction and at the cost of CARRION's life, turned out to be one and the same bartonellosis? And both human and rat leprosy and, more especially the various rickettsioses? Again, what is the position as regards dimorphous mycoses, which are blastomyc

Hippelates, called in Surinam sorro fre-fro ("sore-fly") or eye-gnat, may also transmit conjunctivitis. According to HERMS the insect is, in California, *H pusio* and according to ESCOMEL in Peru, *H [illegible]* Those collected by myself in Surinam belong to the *H currens* *H pallipes* and *H apicatus*

oses to the physician, but not to the mycologist, because these "fausses blastomycoses" are yeasts" in the human or animal body but not in culture?

Let us return to the sores

Notwithstanding the many vernacular names most sores may be classed with either tertiary syphilis tropical ulcer tropicaloid ulcer yaws or leishmaniasis among which may also be classed most boutons e g the *bouton de Bahia* —*de Biskra* and—*de Gafsa* Not so however the *bouton de chaleur* a synonym for prickly heat neither the *bouton d'Amboine*—a synonym for bartonellosis— nor the *bouton des règles*—a synonym for herpes menstrualis nor *fièvre boutonneuse* which, again, is a rickettsiosis (Neither should bouton d Amboine be confused with Ambonese pox i.e yaws) Even in those cases where the name may be considered specific for a certain affection e g., *oriental sore* as synonymous with cutaneous ulcerative or furunculoid leishmaniasis, it is far from improbable that names are interchanged and that for instance, many a tropical ulcer or tertiary syphilitic ulcer is dubbed "oriental sore"

Oriental Jeddah- Bagdad- Yemen- Oasis Rhodesia Biskra Delasoa, Natal Assam Annamite Cochin China and Chiclero (i.e rubber planter") *sores* are apart from being tropical ulcers often leishmania sores, and the same applies to *Sahara chancre herpes du Nil* the *Marmarica* and *Dehli sores* One should not, however confuse Marmarica sore with *Mazzamorra* which is not a sore but an itch, caused by uncinariasis (ancylostomiasis) Neither should *Dehli sore* (spelt with an *h*) a form of leishmaniasis found in India, be confused with *Deli fever* (without the *h*), a rickettsiosis in Sumatra. Or *Sumatra Deli fever* with *Sumatran "Palembangitis* which is synonymous with dengue or "dandy fever" *Herpes du Nil* is no herpes but an ulcerous leishmaniasis One may admittedly contract "solar herpes" ("herpes des Alpinistes") on the banks of the Nile, but this is not herpes du Nil any more than *gâle du Nil* is scabies, for Nilotic scabies" is synonymous with prickly heat. *Gâle des céréales* again is the papulo-vesicular exanthema caused by the pediculoides ventricosus

Leishmaniasis (better trypanosomiasis) too has certain terminological peculiarities One should first of all distinguish between the *visceral cutaneous* or *dermal* and *muco-cutaneous* forms. Despite this sub-

division, the visceral form is sometimes accompanied by dermal abnormalities *kala-azar* means "black skin" because of the discoloration of the face, hands and abdomen caused by the disease. In addition to this, kala-azar may cause *dermal leishmanoid*, or *post kala-azar leishmaniasis* Leishmanoid, as well as kala-azar itself, is caused by Leishmania donovani and not by Leishmania tropica[1] for in the latter case



6. The "bouton" (button) is a typical tropical skin lesion a flat papule centrally covered with a blister which usually turns to ulceration. The "bouton" may be surrounded by an inflammatory erythema. This "bouton" is a "bouton de Boma" epidemically occurring in the Belgian Congo
(Rodhain Antwerp)

dermal leishmanoid would then be cutaneous leishmaniasis, for instance, an oriental sore!

When leishmaniasis affects the mucous membranes—as is especially the case in South America—it is called *espundia* The parasite, *Leishmania braziliensis* is hardly if at all, distinguishable from the two above mentioned members of the species, any distinction having hitherto been made merely on the basis of their respective pathogenetic properties It remains to be discovered whether the parasites in leishmaniasis and espundia, like those in syphilis, yaws and pinta, are identical or not.

[1] This parasite may also set up visceral abnormalities in laboratory animals, *e.g.*, the mouse

We may point out here that many cases in the tropics which were diagnosed as lupus vulgaris or lupus erythematosus were, in fact, cases of leishmaniasis.

Veldt sores and *desert sores* although often found in leishmania locations are often in fact ecthyma, diphtheritic and pseudo-diphtheritic ulcer, tropicaloid and tropical ulcer. The two latter are not synonymous, neither is the former of the two a mild form of the latter, as is the case with *pellagroid* and *pellagra*. *Ulcus tropicum* and *tropicaloid ulcer* differ both clinically and aetiologically. The former is deep and phagedaenic; it is caused by the symbiosis of PLAUT VINCENT, of which disease the Borellia *vincenti*—as if to make confusion more confoun-



The *bouton* (de Boma, de Biskra, de Bahia, de Gafsa) or the Sahara, which here may become a *boil* (Aleppo boil, Bagdad boil, Oriental boil) and subsequently a *sore* that one with perhaps most synonyms of all, Aden ulcer, Cochin China sore, Delhi sore, Jeddah sore, Kandahar sore, Lahore sore, Moulton sore, Mozambique sore, Natal sore, Oriental sore and Pendjeh sore. They are closely related to the chiclero ulcer, endemic granuloma, Nile herpes and other features of cutaneous or muco-cutaneous leishmaniasis, the latter being also termed espundia, bush yaws, etc.

ded!—is also known by the name of Spirochaeta *schaudinni* (in its turn not to be confused with Spirochaeta pallida *schaudinni*). Tropicaloid ulcer, on the other hand, is superficial and hardly phagedaenic, and is caused by the micrococcus mycetoides *castellani*.

Barcoo rot, again, is synonymous with veldt and desert sore. But

jungle rot is impetiginized eczematoid dermatitis, which is far from occurring exclusively in the jungle. And *foot rot* is tinea pedis, and *desert fever* (also valley fever) is coccidioidomycosis!

From Jeddah- Natal Gafsa or Kandahar sore to the *sore mouth of*



8-9 Singapore – or Hongkong foot and Madura foot. The former a superficial, the second a deep fistulous mycosis. Singapore or Hongkong foot is included in the clinical concept of epidermophytosis, which, however does not cover the mycological concept since a great deal of clinical epidermophytosis is not due to the epidermophyton floccosum. Madura foot belongs to the mycetomata and may be caused either by aerobic or anaerobic actinomycetes or nocardiae



Ceylon is, geographically but a step medically however quite a long jump For whereas the former are forms of leishmaniasis, Ceylon sore mouth is tropical aphthosis, and sometimes—though not invariably—identical with *tropical sprue* or *thrush* In *these* cases the English name *sore* corresponds to the German *Soor* (*i.e.* moniliasis) While "Soor"

therefore, is invariably "sore ... sore mouth" need not necessarily be Soor.

The term "tropical sprue" too embraces a mixed concept, covering aphthosis, vitamin deficiency, primary and secondary candida infection, and even (unrecognized) secondary syphilitic angina.

SPRUE < avitaminosis, etc., whether complicated by candidasis or not / primary candidasis

We might be tempted, by this time, to speak of a "snowball" if this chapter were not concerned with tropical diseases. We have been rolling from the sores to the sore mouth, from the sore mouth to sprue, from sprue to candida-infection and thence to the terminology of this fungus, which, so far from being always the cause of the disease, is often merely a complicating factor in many cases of mucosal diseases. For the "sprue fungus" occurs as a saprophyte, or in what is called a "parasite host equilibrium" in which a high degree of infectivity is coupled with low pathogenicity [1] (DUNCAN).

Candidasis is also known under the name of *moniliasis*. Even within this small terminological section there is enormous linguistic confusion: there are more than a hundred synonyms in the candida group alone! [2] At the 7th International Botanical Congress (1950) BENHAM has proposed using the term "candidasis" as a "nomen conservandum".

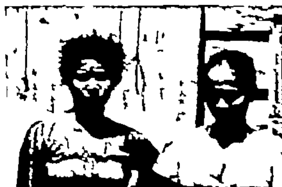
While on the subject of fungi for the second time, it will be apposite to go into the matter further. *Madura foot* (Madura, Madras, India, not the island of Madura, E. of Java) is a mycetoma, but *Singapore-* or *Hongkong foot* is a superficial mycotic infection, *i.e.* epidermophytosis. What is the difference? *Mycetoma* is a deep fistulous mycosis producing granules, as, for instance, in actinomycosis of the jaw and in actinomycosis—or other deep granuloplastic mycoses—of the foot ("Madura foot"). The former is a mycetoma maxillae or mandibulae, the latter mycetoma pedis. Mycetoma may be caused

[1] Meanwhile more and more cases are being described of candida-bronchitis, meningitis and endocarditis.

[2] Most important investigations of this fungus were made in the Netherlands (Baarn Institute) by Dutch women (WESTERDIJK, BERKHOUT, DIDDENS and LODDER).

either by anaerobic actinomyces (formerly also called discomyces) by aerobic nocardia (also classed as actinomyces), or by madurella[1] In non-granuloplastic cases the term *paramycetoma* is used.

Hongkong or Singapore foot, in contrast to Madura foot, is a superficial, infection, usually due to Trichophyton gypseum (a variant of T mentagrophytes) or to Epidermophyton floccosum, the latter term being the only one left over from a number of synonyms no longer in use, such as E. cruris (CASTELLANI) E. inguinale



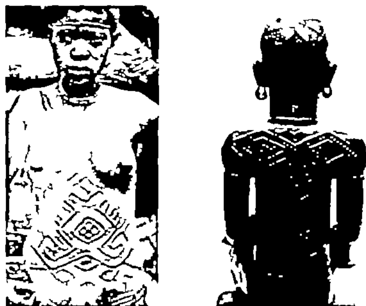
10 Two sisters, the one with crisp hair from a Negro father and a Javanese mother

(SABOURAUD) and E. clypeiforme (MCCARTHY), and from a number of names like E. rubrum, which were classified—*as necessity arose*—with those groups where they belong *e g* the trichophytoneae The epidermophyton, which becomes pleomorphous fairly quickly has in my opinion, also, in that state, been taken for a species by itself and, as such, for the parasite causing *Indonesian pinta disease* which for many years appeared under the pseudonym of *tinea albigena* or (in Indo-China) of *khi hues*[2]

Our viewpoint in this is that the actinomyces (to which belong also the parasite causing erythrasma and the palmellina") should be classed as fungi and not as bacilli. According to this view however both the B. tuberculosis and the B lepræ must also be classed as fungi (note the name *mycobacterium*).

Until quite recently (1927) the pinta disease was taken to be a fungus disease and indeed, the causative (better complicating) fungi were many *e g* aspergillus, penicillium and about twenty more (BRUMPT). The most frequent is assumed to be Dermatium Werneckii.

An interesting detail is that Hongkong or Singapore foot, which is known in Indonesia as *kutu ajer* (*i.e* water louse) and in America as *athlete's foot* is called *priti finga* in Surinam. The term means "lacerated toe" this name, however does not apply to the process involving the tearing away of the entire toe, which, in its turn, is



11 12. Keloid tattoo in the Congo Arts
(Belgian Congo Museum – Tervuren)

known by the name of *ainhum* When priti finga appears on the hand instead of on the foot, it may be a case of "kutu ajer" epidermophyton infection in most cases, however it will be *erosio interdigitalis blastomycetica* or *mycetoruloma*. But still we are not out of the wood no more than priti finga of the hand is bound to have the same causal agent as priti finga of the foot, are we justified in classing *Singapore ear* aetiologically with Singapore foot. For Singapore ear is an otomycosis due to either candida aspergillus penicillium- or actinomycetic infection if not, indeed a pyogenic infectious eczematoid dermatitis (French dermite-épidermite microbienne)

Then there is *mossy foot* not a *fistulous* mycosis such as Madura

foot, nor a *scaly* or *crusty* epidermophytosis like Hongkong foot but a "mycose *végétante*" *i.e. chromomycosis*. The name chromo-blasto-



13. The term "brand" for "mark of quality" originates from irons like these, by which slaves (the "*ebano vivo*") were marked. When the "living ebony" showed some skin disease or other "damage" the slave was called a "macron"

(Simons Sr – Amsterdam)

mycosis is also often used but chromomycosis is no true blastomycosis. Mossy foot may also be due to pyoderma vegetans as well as to lymphostatic verrucosis in filariasis Bancrofti or it may "merely"



14. "Make-up tattoo" of an Indian woman from Goajira (South America)

(Rius – Caracas)

be crustous yaws, which can be cured by neoarsphenamine or penicillin. To some extent it is probably the same as *craw craw*, *i.e.*, according to GOUGEROT pyoderma vegetans, and, therefore, not—

or not always—*gale filarienne* unless one wishes to class with this pyodermatic mossy foot, which is sometimes regarded as a complication of filariasis BANCROFTI

But there are many more of these "feet" and even "legs" *Happy feet* or *jittery legs* are the *burning feet* or *dedak legs* in vitamin B_2 deficiency *Castellani legs* are those with purulent folliculitis (often coupled with jungle rot) *boomerang legs* are the saber tibiae in yaws *black legs* are caused by anthrax infection and the *rose legs* of Surinam are due to



15 These "artefacts" may have two purposes *a* a form of maltreatment or other effect "*in effigie*" doing harm or "making love" to an image, representing an absent or unattainable person *b* spurring on an idol to answer the prayers.

the erysipelatous infection of filaria legs whether or not (yet) elephantiasically enlarged They are also known under the names of *bigi futu*, *Barbados legs* or *elephantiasis arabum* (in Indonesia, *kaki* (= feet) *gadja* (= elephant)

Big heel is probably a form of gunduh. *Elephantiasis graecorum* is elephantiasis in leprosy *elephantiasis nostras* is perhaps caused by chronic erysipelas and, in this case, more or less akin to *elephantiasis pyodermatica* Filariasis attacks, apart from the legs also the arms and genitals but the term *elephantiasis genitorectalis* is used to denote *esthiomène* or

the *genito-anal-rectal syndrome* of JERSILD in lymphopathia venerea. In support of HUGUIER, French dermatologists contested the correctness of JERSILD's term for esthiomène, but the most confusing fact in this controversy is that the syndrome is also known—utterly wrongly in fact—by the name of *syphiloma anorectale* [1]

With this we have arrived, by devious ways, at one of the most perplexing spots in the dermatological jungle. *Lymphogranuloma inguinale* or NICOLAS FAVRE DURAND's disease (which, by the way, is not a granuloma at all) is often mixed up with *granuloma venereum*. The former is a virus disease (*i.e.*, if one classes the para rickettsiae as viruses), the latter is caused by Klebsiella granulomatis, formerly called DONOVAN's capsule coccus. For this reason it is better to speak of lymphopathia venerea or of the disease of NICOLAS FAVRE, as distinct from granuloma venereum of MACLEOD and DONOVAN. (The Germans call the former "climatic bubo".)

Apart from the large number of different sores, "feet" and "legs" there are also a great many "itches" which are well worth close inquiry. Some of these itches—although sometimes wrongly diagnosed—must be regarded as synonymous with pruritus in dermatozoonoses and epizoonoses. By *dermatozoonoses* DARIER understands zoonoses in which the insect dwells in the skin, as in scabies and chigger; epizoonoses he calls those diseases in which the insect does not bore into the skin, as in pediculosis and phthiriasis. These definitions are not entirely adequate, since in those cases where a given microbe is brought into the body by a bite or a sting we do not speak of zoonosis but of infection, as, for instance, in rickettsiosis, in leishmaniasis, etc. Epizoonosis, therefore, is a skin affection—in some cases probably allergic—caused by the sting or bite of an insect *without* this insect introducing a micro-organism into the victim's body. At the same time it is far from impossible that itch precedes the actual infectious disease transmitted by the insect (*cf.* *verruga* and leishmaniasis).

Itches are sometimes dermato- but more frequently epizoonoses, *e.g.*, as a result of pediculoides and trombiculae. In other cases, itches are either the "porte d'entrée" if not, indeed, the local, focal, or

[1] By syphilomata and syphilitic bursitis are also understood: juxta-articular nodes (or tropical xanthomata!)

even universal allergic reaction to uncinariasis (ancylostomiasis) to the cercariae of schistosomiasis [1] etc. In yet other cases itches are caused by a mycotic infection, as in *jockey's* or *dhobie* (*i.e.* laundry man's) *itch* which we have described above as kutu ajer and Hongkong foot. Apart from dhobie itch there is also *dhobie mark itch* caused by marking ink made from the anacardium or cashew nut.

Apart from dhobie itch of the toes there is, again, *toe itch* which, however is the "porte d'entrée" of ancylostomiasis. The same applies to *ground- miner's* and *swamp-itch*. Toe itch, in its turn, differs from *mango toe* which is another synonym for Hongkong foot. Whereas "laundryman's itch" is an epidermophytosis, the same is not the case with "laundrywoman's hands" which is a tylotic eczema, nor with *water itch* which is synonymous with (maybe allergic) schistosome dermatitis, as are also *swimmer's* and *collector's itch*. And while the dhobie, in common with the Singapore Jockey has apart from "ink-dermatitis" epidermophytosis as an occupational dermatosis the coolie lent his trade name to the schistosome dermatitis called *coolie itch*. (But Dr COOLEY gave his name to familial erythroblastosis.)

Schistosomiasis causing water- swimmer's- collector's and coolie itch differs from the form known as *bilharziasis*. For although schistosomata MANSONI as well as schistosomata haematobia or japonica may set up itching urticaria or even dermatitis, it has been shown that swimmer's itch is often caused by a "non human" species of parasite which is found not only in the tropics but also in certain parts of Europe. In such cases we have to do with a strongly itching affection of longer duration, and of an erythemato-papular or pustular or sometimes, maybe evanescent urticarial nature localized chiefly on the arms and legs and caused by the penetration of cercariae into the skin (*e.g.* C. ocellate or C. longicauda). In the case of the urticarial form an allergic reaction must also be suspected. (Most cercariae develop in *Planorbis* and other genera of snails.) Again Florida coast *Seabather's eruption* (SAMS) is not (yet) identical with swimmer's itch, because the former is probably due to another marine organism. (Neither is it identical with jelly fish dermatitis.)

[1] OLIVER, American Journal of Hygiene 1949



(*a*) Crisp hair of a Negro



(*b*) Straight hair of a blond Dutchman in South America.
(Note presence of piedra)



(*c*) Thick straight hair of a Caribbean Indian



(*d*) Thick straight hair of an Eurasian.
(Half Dutch half Javanese)

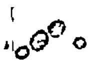


(*e*) Thick hair dominantly straight in a man of a Negro mother and Chinese father.



(*f*) Thick hair dominantly crisp in a man of a Negro father and Javanese mother







(*g–i*) Sections of straight and crisp hair. Note various forms. No. *h* was taken from a Caribbean Indian.

16 (a–i). Some samples of hair from the author's collection.

Sawah itch is schistosome dermatitis of the Malay countries.[1]

To mention a few more itches: *Cuban* or *Philippine itch* is identical with alastrim (variola benigna). *Copra itch* is an epizoonosis caused by the copra mite (tyroglyphus longior). The fact that the copra mite dwells in the copra plant should not lead us to conclude that the "batatas-louse" (sweet potatos-louse) lives on the batatas plant, for this trombiculum flui et vanommereni owes its name to the fact that the pruritus (and pyoderma) which it causes, most frequently affects those members of the white population (called in Surinam "patatta") who have only just arrived in the tropics, and who are evidently still sensitive to the bite of this trombiculum. The insect is related to trombiculum autumnalis, also called *aoûtat* (from the French for August, when its activity is most intensive) or *rouget* (after its colour).

Yet another itch is *malabar itch* (after Malabar in Madras, India) *i.e.* trichophytia superficialis. *Bedouin's itch* is prickly heat also called *lichen tropicus* (a lichen which, instead of being papular is usually either bullous or vesicular); it is the same as *calori* with the Italians, *milliaires papuleuses* with the French, and *rode hond* (roter Hund, *i.e.* "red dog") among the Dutch and the Germans. It is a tropical disease, which, however, is also found in moderate climates, (*e.g.*, among warmly dressed stokers and firemen), and it has the curious feature of attacking whites in preference to the natives of the tropics. The disease has nothing whatever to do with rubella or rubeola, which is also called "red dog" in Holland; neither is it identical with that papular exanthema resembling prickly heat, which may affect persons sensitized to light by the virus of NICOLAS-FAVRE's disease (see chapter 31).

At this point we would also mention *harara* (which, as it happens, also means "heat") a Palestinian disease resembling strophulus and sometimes even scabies, and caused by the bite of the Phlebotomus, which insect we know as the transmitter of leishmaniasis and bartonellosis.

[1] In a number of cases—especially where haematobia are involved—there is pseudo-elephantiasic enlargement of the penis, or an excrescence resembling condyloma acuminatum at the anus, called *bilharzioma*. Not only should this bilharzioma be held distinct from haemorrhoids and from condylomata acuminata proper (maybe, too, from condyloma latum, but this requires a considerable degree of imagination), but, more particularly, from *amoeboma* in amoebic dysentery.

Prairie itch of all itches, has the most comprehensive signification, the name being used for all sorts of eczemas caused by plants, and epizoonoses

As regards the former *(eczemas caused by plants and herbs)* confusion threatens between jungle dermatitis allergic plant eczema, and "phyto-photo dermatosis all of which will be described later.

Another name which one often comes across, but which is applied to different diseases is the collective name *pox*" In Dutch this means variola but it is also a popular or vulgar name for (secondary) syphilis. Variola is called *small pox* and varicella is called *chicken pox* (English) and *water pox* (Dutch[1]).

✓ *Milk pox Kaffir pox* and *Samoa pox* are mitigated variola, and are also known as *alastrim varioloid* (*varioloïs*) and *variola minor* A less well-known name for the same disease is Philippine itch or Cuban itch (already mentioned above) Further there are "*monkey pox*" (Dutch *apenpokken*) so called because of the rapid spread of the disease[2] and synonymous with MANSON's pyosis or impetigo bullosa tropica *rickettsia pox Spanish pox* (secondary syphilis) and *Amboinese pox* an obsolete term for yaws. *Black pox* again is haemorrhagic variola, and *para-pox* (paravaccinia) is "milker's nodules" but also denotes the telangiectatic papules forming at the place of vaccination. Maybe, indeed, that paravaccinia is not a type of variola at all but a symptom of infection with LIPSCHÜTZ' strongyloplasma.

Opinions sometimes differ as to whether the word *variola* is singular or plural linguistically however, it is singular otherwise we should have to speak of variola maiora, or variolae maiores. The French distinguish between *grande vérole* (*i.e.* syphilis) *petite vérole* (variola), and *petite vérole volante* (varicella).

When mentioning "monkey pox" we referred to *pyosis* In this connection we may observe that, apart from MANSON's pyosis, we also know CORLETT's pyosis (bullous staphyloderma) CASTELLANI's

Fowl pox are *mollusca contagiosa* in poultry Sheep pox or orf are viral pustules in sheep and rarely in man (Fig. 109)

The Japanese name *tobihi* means "spreading like wild fire" It is interesting to note that alaster" (*alastrim*) also means "dissemination by leaps and bounds" The Red Indian name *rara* for tinea imbricata means "the flying disease " "blown over" by the enemy

pyosis (jungle rot) and tropical pyosis synonymous with ecthyma.

The terminology relating to *leprosy* is less complicated than that of pox, because by leprosy we understand today only the disease caused by HANSEN's bacillus. Names such as *lepra asturica*, *lepra lombardica* (both meaning pellagra), *lepra albas* (for psoriasis) etc. have become obsolete. Even in its more restricted meaning the term "lepra" has changed during the last few decades: we now distinguish, in addition to the malignant form, rich in bacilli and containing *lepra cells* ("lepromatous leprosy") the benign (tuberculoid) form which contains few bacilli and no lepra cells. This is of great importance for the epidemiology of the disease and for the problems of therapy and isolation. It used to be thought that there was an intermediate form, *lepra mixta*—despite the fact that, in leprological terminology "lepra mixta" really means a sub-type of the lepromatous form. Still there are some rare cases of the combination of a lepromatous and tuberculoid process in the same individual, which again should not be confused with bacillary positive or "major tuberculoid" leprosy. Uncertain, not fully determined cases are now called "I lepra" "I" being short for "indeterminate" (International Lepra Congress Havana 1948).

Yet another "classical" name which may be explained in various ways is the word "*carbuncle*". While this may denote a deep pyogenic folliculitis or mass-furuncle there are also the *plague* and the *anthrax carbuncle* (*Pestis siberiana* is another name for anthrax.) Moreover the English word "*boil*" which means furuncle, is also frequently used to denote the furunculoid in cutaneous leishmaniasis (*cf.* oriental and Aleppo boil).

We have so far dealt with a number of names which are seemingly synonymous: there are, however, certain names that are homonymous or nearly so, *i.e.* they sound (almost) alike but have different meanings. Of these, we already mentioned *buba* (filariasis), *bubul* (yaws) and *bubab* (yaws but also leishmaniasis). We also mentioned *gundu* and *goundu* in which case it may be said that one was derived from the other. Then there is *piquota* (synonym for pinta) and *pique* (synonym for tunga penetrans); *Q fever* (a rickettsiosis) and *Quintana fever* (dengue). *Taches bleues* are small blue spots on the abdomen and in the sides in phthiriasis but the *tache bleue sacrée* is the *blue button* or Mongolian

spot, a deep naevus in the lumbar region (sacrum or buttocks) of newborn childern of the Mongolian race [1] (The Japanese imagined that these Mongolian spots were the finger prints of the divinity on the Japanese race When it was discovered, however, that the Mongolian spot may also be found on certain monkeys this Japanese legend soon lost its authenticity) Again, there is the *blue disease i.e.* Rocky



17 Despite the Latin name efflorescence (flos = flower) for lesion dermatological terminology is not flowery This is the mossy foot, a tropical disease chromomycosis. Lymphostatic verrucosis and leishmaniasis may produce a similar condition. (See also Fig 59)

Mountain fever and *morbus coeruleus* or blue jaundice" *i.e.* cyanosis in congenital vitium cordis We have already mentioned *black disease i.e.* kala-azar *tache noire* however is the primary lesion in tick-bite typhus *Red fever* is a little used synonym for erysipeloid, and *Congolese red fever*

[1] The Mongolian spot has also been observed on Negroes and among certain Slav tribes.

for certain types of rickettsiosis. Dengue, a variant of *yellow fever* is also called red fever. It is the virus disease transmitted by Stegomia calopus.

Confusion is also possible between the *sandfly* and the *sandflea*. The former is Phlebotomus papatasii, the winged insect that transmits the leishmania infection; the latter is the chigo, jigger or sika (sarcopsylla or tunga penetrans) which burrows into the skin of the sole of the foot and causes intense irritation but no disease.

It may be better to steer clear of philology; the origin of the words is alone well worth studying. We may, however, cite one or two examples.

We already mentioned the occurrence of "twin words" like craw-craw or kro-kro. The latter is probably an *onomatopoeia* derived from kr krr—the sound produced by scratching. One is also reminded in this connection of the Negro-English term *kras krassi* for itch, or scabies.

Despite the many efflorescences (flos = flower) dermatological language can hardly be called flowery. *Muguet* (*i.e.* lilies of the valley) is the French name for the white spots (aphthae) caused by thrush, not the spotted song bird but candidiasis or moniliasis. These lilies of the valley, in fact, also grow in the tropics, and by the time they wither away, we have arrived at the German word *Soor* (sohren = German for to wilt, to wither). To pass on from flowers to fruit, there is the *date sore* (for leishmaniasis[1]), *mango toe*, *durian sore*, *roosbeen* (erysipelas) in filariasis side by side with *mal de la rosa* (synonym for pellagra), *keembang keringat* (= sweat flowers") for miliariasis, *panu kembang* (= panu flowers[2]) for corymbiform tinea flava, and *cayenne pepper spots* for the patches occurring in purpura. While *framboesia* (= raspberry) is the latin name of yaws, *mulberry rash* is the rash in typhus, while *granuloma frambesiiforme* is synonymous with pyogenetic granuloma or botryomycosis (q.v.). *Flower yaws*" denotes the corymbiform eruption of small yaws papules.[3]

The word *lichen* means moss, but *mossy foot* (chromomycosis) is not

[1] *Fièvre de dattes* is dengue, which occurs during the date harvest.
[2] Also *panu bunga* in Malaya.
[3] *Crab yaw* affects the soles of the feet and makes the patient walk like a crab.

lichen in the dermatological sense of the term, which denotes the appearance of a group of papules, while *tropical lichen* (miliariasis) again, is characterized by the appearance of *vesicles*[1] A *mango-* or *mango toe* is tinea of the foot called after the tropical mango fruit (Magnifera indica) for some unknown reason, *Mango dermatitis* is angular stomatitis said to be due to irritation by the juice from biting into the fruit, but most probably it is often pellagra – per lèche still *mangy* is the native name for a chronic enlargement of the parotids, which occurs in Madagascar (Also in other regions of Africa and in Brazil.)

Some flower-names have animal names as synonyms *e g* kembang keringat (sweat flowers") = Dutch "red dog" (prickly heat) panu kembang ("tinea flava flowers") and *tingifowroe hatta* (tingifowroe meaning carrion vulture" or "stink bird") or *taja futu* (turnip foot) and *elephantiasis* Taja futu (see Vol. II) is a form of elephantiasis characterized by papules and vegetations "Taja" is the Negro-English name for the tuber root of Xanthosoma sagitti folium, a popular vege table food. The French word "muguet" (see above) is synonymous with langue du chat" (cat s tongue, *i.e* monilia stomatitis)

A Negro suffering severely from vitiligo pinta or other depigmentation trouble is called *leopard man* but also "*letter-wood skin*" after the spotted South American species of wood Brosimum discolour or Piratinera guianensis, the kind of wood from which the Red Indians make their bows

Animal names are *apenpokken* ("monkey pox" already referred to) *elephantiasis* *kutu ayer* (= water louse) *leopard man* (vitiligo and pinta disease) *kodal anjing* (*i.e* spotted dog) for leprosy *cockroach bite* for herpes(?)[2] and *facies leontina* in leprosy We also find the name "lion in *sakit singa* (lion s disease, a Javanese name for syphilis) Since no lions, however are found in Indonesia, we may observe that the sanskrit word singa = lion, or "strong" dates from the Hindu period lion s disease" or "the strong disease" therefore, is syphilis *i.e* sakit singa. (But if the patient has a 'lion s face" (*facies leontina*), he has

[1] Unless, that is, lichen tropicus is held to signify exclusively the papular form of prickly heat but even in that case the papules are much too disseminated to justify applying the dermatological term "lichen"

[2] or Quincke s oedema? See also Chagas disease.

lepromatous swelling of the skin in leprosy) In the place of *sakit* one sometimes sees the word *radjah* which does not mean prince (radja without the *h*) but "dirty" (sanskrit) and, in that sense is also synonymous with both menstruation and illness in general.

This leads us to yet another example. Camel hair eczema occurs fairly frequently outside the tropics it is not a tropical eczema" for



18 The tropical *kr* is identical with the sailor's skin Particularly non-tropical individuals reveal a tropical skin. The tropical *complexion* is due to vitamin-B-complex deficiency

camel hair as used to make brushes, actually comes from squirrels. (And the essence d Orient" used to varnish artificial pearls, does not come from the Orient, but is made from the scales of European fishes)

Yet another range of diseases are called after worms as *ringworm* for all kinds of tinea *ringworm yaws* for circinate yaws *screw worm* for the larva of the cochliomyia fly the *mosquito* worm (French *ver macaque*) for the larva of Dermatobia the *ver du Cayor* (cayor worm)

for the larva of Cordylobia the *pichi bichi* or rainworm of the Antilles for urticaria the *Guinea- or Medina worm* for dracontiasis, and the *boassi (worm)* for leprosy It will no doubt have struck the reader that, among all the names mentioned so far there *is not* one that specifically expresses something relating to the tropics themselves, with the exception of those affections which are denoted by the adjective "*tropical*" (*e g* tropical ulcer) or with the cosmopolitan adjective "*solar*" (as prurigo solaris) or *actinic* (as actinic cheilitis[1]).





19 The "four tissue organ", the nose is place of predilection for tuberculosis, syphilis, yaws leprosy leishmaniasis, klebsiella-infection, etc. Sometimes the skin may become thickened as is seen in leprosy and sometimes the bone as is the fact in goundou and rhinoscleroma. On the other hand destruction may follow lupus and espundia, and may cause the high syphilitic and low lepromatous saddle nose and even gangosa.

Even *tropical skin* is not really a tropical disease for it is synonymous with sailor's and farmer's skin, a condition comprising lichenification, dryness, hyperkeratosis and freckles due to prolonged exposure to the weather and the sun. In fact this dermatosis is a *heliopathia i.e.* a disease caused by the sun, and not a *heloderma* because a heloderma is a poisonous lizard found in Mexico

[1] Actinic implies "sun's rays" but in actinomycosis "ray fungus"

The operative word "helios" is still represented in *ephelis* (freckle).

It is important to remember that medical language is still further complicated by the fact that some peoples are averse to pronouncing the names of their diseases, because it might be at the same time the name of some deity (*cf.* also the Jewish custom of substituting the name ADONAI for Jehovah). If one cannot get away from pronouncing the name in question one must "touch wood" or give oneself a tap on the mouth in order to avert disaster. In Surinam the term *takru siki* (= the "ugly disease") is used to denote leprosy [1] and when the Surinam native mentions that a relation or a friend "has been kicked by a donkey" ("burichi skoppu him") one is expected to infer that the patient in question has an attack of filaria fever—a disease which the Surinam native as stubbornly denies having as most whites deny having scabies or favus. (See also page 146–147.)

✓ Some Indonesian tribes even go to the length of changing the patient's name too, in order to mislead the evil spirits (and, incidentally, the epidemiological service as well). This ostrich's policy has its antipodal complement in customs such as the "*guna guna*", a superstition by which an attempt is made to give an enemy a disease by pronouncing the name of the disease selected for the purpose, while at the same time lacerating a dummy which is to represent the hated person. This is similar to black magic in Africa where the witch doctor conjures up images of persons who are to be attracted or destroyed. Both actions constitute a form of fetishism. A stab in the liver may cause the victim to fall in love with someone, a stab in the heart is intended to cause his or her death. (I was called to a case of pigmentations in a Chinese, who had been bewitched in such a manner, but close observation revealed the fact that he was also being poisoned with arsenic.)

But is such magic practised only in the tropics? Surely "throwing balls" and target shooting at the images of enemies is not so very different from this so-called "*executio in effigie*".

While masks, and tattooing may serve, on the one hand, to make the patient unrecognizable and camouflage him against evil spirits,

[1] (also tuberculosis). *Siki* (from "sick") is similar to *nsiki* in South Rhodesia where it is used to indicate syphilis.

it is also seen that masks are used to represent a disease. Thus, the ruby in the Indonesian mask frequently symbolizes an ulcer or furuncle. We have now arrived at the end of our itinerary for the trip through the jungle of tropical dermatology a territory containing many other surprises apart from terminological ones especially because we shall come across diseases which we should not have expected to find there.



20. Consecutive achromia is not merely the result of a "screening effect" by scales or crusts as is seen in this case of achromia in secondary yaws. See also Fig 24 and 25 and chapter 4 and 19

Consider for example, the importance of tuberculosis of the skin of allergy [1] and of what are sometimes called the "ids"! How tempting it is to compare the superficial calabar swellings in loa loa filaria with the nodes in onchocerciasis or volvulosis while the former are sometimes an allergic reaction, a Quincke's oedema whereas the latter are connective tissue nodes, i.e. cysts containing microfilariae

N.B The Mitsuda and Frei reaction, allergy to the ascarides in schistosomiasis, filariasis, hypersensitivity to light caused by lymphopathia venerea, etc.

Again we must beware of the opinion that certain peoples or tribes are naturally immune to certain diseases, as used to be (and still often is) thought in respect of leprosy and filariasis in the Caribbean islands and in respect of sarcoids among Negroes. Is the sarcoid of BOECK among Negroes identical with that among whites although, as we know the sarcoid tissue structure is practically a non-specific reac-

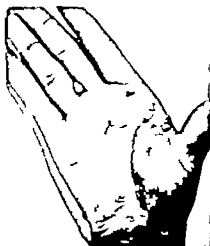


21 A legendary disease: tinea albigena. This form of pinta or vitiligo was regarded as a fungous disease because of the presence of secondary invading epidermophyton of which the pleomorphic stage was not known at the time of its publication and was regarded as a newly discovered fungus

tion? Is lupus erythematosus in persons from territories where leishmaniasis is common, "erythematosus-leishmaniasis" or a leishmanoid erythematosus?[1] Why does psoriasis disappear when the patient goes to the tropics, and why—one may just as well ask—is it not true to

[1] SIMONS, Doc. Neerl. et Indones. de Morb. Trop. 1949

say that that cures him? How is it that acne rosacea is practically unknown in the tropics? Is there such a thing as anhidrotic asthenia caused by chronic prickly heat? Is piedraia not, in fact, piedra, and vice versa? Is "achromia" or "pseudo-achromia parasitaria" or "secondary pseudo-achromia" merely the result of a "screening effect" seeing that thick squamae and crusts have little or no such "screening effect"? Is phagedaenismus merely a concomitant of



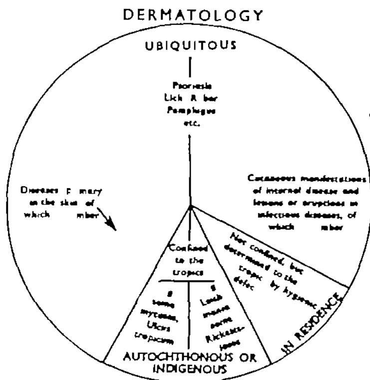
22. Kaposi's idiopathic haemorrhagic sarcoma is now frequently reported in the tropics. Is it a newcomer or has it formerly been overlooked or misdiagnosed?

(Berens, Degest and Babbit-Cameron)

fusospirillary symbiosis, and, if so, how does one explain the existence of pyogenic and even amoebic phagedaenic ulcers? And why are pyogenic ulcers sometimes and sometimes not, phagedaenic? What is the action of the Hippelates in yaws and pinta? About what aspects of the problem are we still in the dark, what are the still unexplored fields, how much of what we know consists of relics from out-of-date science—as, for instance, the prodomi of leprosy and tinea albigena?

And frankly speaking, how many cases of pinta are in fact mere "vitiligo-in-syphilitics"? Has KAPOSI's idiopathic haemorrhagic sar

coma always been in the tropics only discovered due to modern science, or is it a criollo [1] and no blastoma but an infectious disease? And what about SENEAR USHER's SYNDROME which is now quite frequently reported in the tropics?



Indeed we may well ask, where does the jungle of tropical dermatology begin where does it end nay where is one to look for its location? In short, is there such a thing as a science of pure tropical dermatology?

A "criollo" is an offspring born from pure white ancestors in the tropics (South America). However the name has also been applied to mulattos and mestizos and to all forms and relics of "import"

C. DERMATOLOGY IN THE TROPICS AND TROPICAL DERMATOLOGY

Now the most important question that arises when we speak of "tropical dermatology" is surely what exactly are we to understand by "the tropics" and what by "tropical disease" for there are several relevant factors to be taken into account, as for example,

1. whether the climate is hot and dry or warm and moist (humidity rainfall)
2. whether we have to do with coastal, or with mountainous regions
3. regional differences, e.g. those marked by the prevalence of specific genera of insects which function as intermediary hosts
4. racial differences also in living habits, clothing diet, etc. between immigrants the autochthonous population and mixed races

All these conditions may vary considerably within comparatively small regions of one and the same country It is not only that, in Indonesia, the palm grows at the foot of the mountain capped with the eternal snow but within an area the size of the Netherlands some people try to alleviate their tropical prickly heat by seeking, night and day the coolness of the fans and air-conditioning (for instance at Jakarta) while others eat strawberries and sleep under blankets (as at Bandung)

There are tropical regions, as, for instance in Africa, where loasis and dracontiasis occur owing to the local presence of the intermediate hosts chrysops and cyclops whereas the vectors—and also therefore, the diseases—are either lacking [1] or becoming extinct elsewhere, as in Java. This was also the case with the Medina worm disease of the African Negro slaves in Surinam and in the Antilles A typically tropical disease yaws, is far more frequent in wet regions than in parts with a low rainfall. It is for instance, not autochthonous in Curaçao (dry climate) but it is in Santo Domingo and in the Windward Islands (wet climate) (AARS)

There are also parts where the factor determining the epidemic

[1] It is obvious that isolated cases here and there do not invalidate the notion "lacking"

character of a disease is not the tropical climate as such, but the soil (*e g* sand and the presence of chigoes (*i.e* tunga penetrans))

There may be *probable racial differences* to account for the fact that the white man is more liable to contract prickly heat than the native. There are also pseudo-racial differences (footwear) which render the white man less liable to tropical ulcers than the autochthonous population there are genuine racial differences which explain why a bearded European in Europe may contract trichophytia profunda



23 Freckles in the Negro On the nose a "plokko" *i.e* keloid forming acne vulgaris.

while his beardless fellow in the tropics only gets trichophytia superficialis And finally there are racial differences which often prevent the physician from noticing something which is definitely present *i.e* erythema in a dark skin

What precisely *is* a tropical skin disease? Is it a skin disease which is most prevalent within the torrid zone between the tropics of Capricorn and Cancer? In that case impetigo would surely be a tropical skin disease. Or are there really no tropical diseases, seeing that practically all of them have been found at some time or another in colder regions as well? Is the giraffe not a tropical animal because

giraffes have sometimes been born in Europe? Is the palm not a tropical plant because it also grows in certain parts of Europe? Is plague a tropical disease because it occurs only in the tropics and *was* it formerly *not* a tropical disease when it ravaged Europe in the Middle Ages? What about pellagra, that gipsy among diseases, which wanders wherever it is allowed to flourish? Is infectious eczematoid dermatitis a cosmopolitan staphyloderma, and jungle rot—practically the same thing—a tropical skin disease? Is Deli fever a real tropical disease



24 Panu or achromia parasitaria from tinea versicolor in Javanese.



25. Consecutive achromia is not only seen in tinea versicolor yaws, etc. This is a case in eczema in a Javanese.

because this, let us say tropical form of the almost ubiquitous rickettsioses bears the name of a tropical region (Sumatra) while its "sister diseases" Rocky Mountain fever and tsutsugamushi fever occur in colder climates?

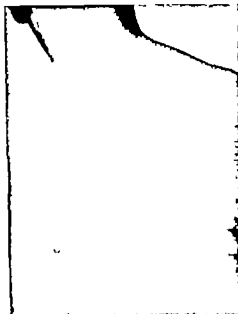
It is so difficult, in short, to give a proper definition that we shall

content ourselves with the following very general one *a tropical (skin) disease is a disease which by virtue of its aetiology occurs either exclusively or predominantly in some tropical or sub-tropical region where though not strictly endemic it is either autochthonous or in residence since it has been repulsed in other areas by hygienic measures*

In this section we shall give a *general survey* of the skin diseases of the tropics both among the native and among the white population, and both in the warmer coastal regions and in the colder mountain districts in so far as they are not described in other parts of the book

For the sake of convenience the order of sequence will be kept as far as possible alphabetical, without, of course, entirely disturbing the basic mutual connections while those diseases which form the subject of a special chapter in the book, have been omitted from this survey

Achromia is very frequent in the tropics Apart from albinism and vitiligo, achromia may occur in pinta, leprosy and as a consequence of certain dermatoses as, for instance, after psoriasis when it is called *consecutive achromia* The most common form is achromia parasitaria caused by tinea versicolor often, however leukoderma is set up in the dark skin after eczema or after yaws Whether this type of achromia is caused by a screening effect against the sun s rays must be doubted, since it is also seen around the scales This form of achromia is also lighter than perinaevic vitiligo or Sutton s disease, in which vitiligo appears around naevi and lentigines. Whereas in achromia parasitaria or secondary achromia, there is no loss of pigment in Sutton s halo naevus there is depigmentation. (See also in the relevant sections in this chapter and in other parts of this book.) The achromia following yaws is *not* akin to pinta leukoderma, nor to the primary collier de Vénus in syphilis. Pintoid yaws" is the inadequate(?) name for pinta with juxta-articular nodules The term implies (perhaps incorrectly) the combination or even the identity of yaws and pinta. In the Buaki disease, and in Diboba in the Belgian and French Congo there is depigmentation and oedema, probably due to malnutrition from cassava diets and anaemia due to hookworm disease, depigmentation being most noticeable in the face The hair loses its gloss and becomes straight and dirty" In my opinion



26. A "white spot disease" – white atrophic spots as seen following varicella or prickly heat.



27 White atrophic spots due to caustics used for the removal of freckles.

this condition is one of the pellagra group (see "kwashiorkor" in the chapter on pellagra). See also vitiligo and drug eruption, as well as the chapter dealing with achromia.

Acne vulgaris is extremely frequent in the tropics and strikingly more so among whites and the half breed races than among the natives. There is no doubt that one of the contributory factors is the sufferers' diet, which is rich in carbohydrates (rice) and their fondness for sweets. An interesting point is the favourable influence of the B_2 vitamin complex in the treatment of acne vulgaris. Although Negroes are less troubled with acne ("*pukkie*") than the white and coloured races, they are not by any means free from the affection which, indeed, may give rise to ugly keloids. By *tropical acne* we mean acne with atypical localization. It appears more often than not on arms, shoulders and back, in combination with the facial affection. "*Oil-acne*" is of infrequent occurrence, chiefly among aeroplane mechanics, but rarely in the actual oil refineries.

An altogether different case is that of *acne rosacea*, a dermatosis of great frequency in Europe, but rarely met with in the tropics either among whites or among the natives. A Javanese, Sundanese, Negro, American Indian, West Indies or East Indies half breed with acne rosacea is a great rarity. "Imported" whites are sometimes less troubled with it than their direct descendants.

Could rosacea be a tuberculid (BEINTEMA) and for this reason, in common with most tuberculids, occur only infrequently in the tropics? One sometimes sees whites or Creoles in the tropics who towards middle age, develop telangiectasiae in the face, lower jaw and neck, which however does not correspond to the classical disease picture of rosacea.

The fatty skin called *kerosis* (DARIER) which is almost typical of both whites and coloureds in the tropics is often accompanied by a "*tropical complexion*", i.e. a yellow, dull colour of the skin, characteristic of the white man or woman who has lived many years in the tropics. The cause of this peculiar complexion is unknown. It has been attributed to lack of ultraviolet radiation due to the person's habit of avoiding the sun and always seeking the shade, to excessive moistness of the skin, and, more recently, to the lack of certain

vitamins of the B_2 range In the latter case the affection is part of the "seborrhoeic state which will be described further on in the section dealing with disorders due to malnutrition.

In children, the tropical complexion is sometimes coupled with a slight prognathism, *i.e.* projection of the lower jaw To call tropical complexion a form of anaemia (*fausse anémie tropicale infantile*) may cause confusion with genuine tropical anaemia, a collective name for



28 Tension alopecia due to excessive combing of the hair (*Jelliffe-Ibadan*)

anaemia caused by malaria, ancylostomiasis and many other factors

Livedo racemosa as a vascular disease, sometimes occurs in the tropics, also in mountainous regions as a result of the increased formation of cold agglutinins in the blood (*e.g.* in virus pneumonia)

Acrodermatitis (HALLOPEAU) I came across one case in Jakarta in a Dutch child of 11

Actinomycosis of the jaw is found in the tropics at Surabaya, I saw a Javanese with a distinct ligneous phlegmon caused by chronic actinomycosis [1] There was a similar case of a Javanese soldier at Jogja.

[1] SIMONS, Artsenkring (Physicians Circle) Surabaya, Dec. 1938.

It is interesting to note that actinomycosis of the jaw is rare in many tropical regions, while actinomycosis of the foot, on the other hand, is practically unknown in northerly territories. Mycetoma of the foot—usually nothing more or less than actinomycosis pedis—has become a tropical concept" (see also the relevant chapter)

Adenoma sebaceum too, definitely occurs in the tropics We saw one case in an Indo-Chinese soldier at Jakarta, a soldier of mixed breed there were no neurological nor psychic phenomena.

Addison s disease This was met with in a Chinese in Paramaribo

Allergic dermatoses are dealt with in Vol II See also page 67

Alopecia areata is quite rare in the tropics, also among whites I once saw a negress with alopecia areata of almost the entire occiput (serology negative) There is an alopecia which may be caused by the hair being combed too rigidly as is shown in Fig 28 Folliculitis decalvans is fairly frequent. This scarring alopecia should not be taken for syphilitic alopecia nor for alopecia areata. Permanent alopecia limited to the lateral parts of the scalp caused by sickle cell anaemia was described by CORNBLEET SCHORR and BARSKY Arch of Dermat and Syph. (1949)[1] (See also Fig 31 and the paragraph on syphilis.) A form of malignant alopecia from atabrine intoxication has been reported by SCHAMBERG (Journ. of Invest. Dermat 1951)

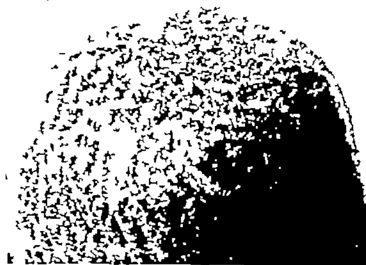
Amoebiasis cutanea caused by Entamoeba histolytica, is characterized by a large superficial *amoebic ulcer* or by an *amoeboma* of the genitals (STRAUB HEILBRUNN KEIZER) or on the anus The ulcer may assume large dimensions but heals comparatively quickly with emetine therapy It should not be confused with carcinoma, nor be taken for a syphilitic process

WITHERSPOON described a case of amoebic dysentery with exfoliative dermatitis which was soon cured with emetine Cutaneous reactions in amoebiasis revealing urticaria, Quincke s oedema papular rashes and pruritus have been reported since 1911 (MILLENEY) These reactions do not show amoebae but they are said to respond to emetine

[1] Sickle cell anaemia or HERRICK s disease is dominant hereditary disease in the Negro revealing a triad of anaemia, spleno- and hepato-megalia and ulcers of the legs, which are usually located on both internal ankles. The surrounding skin is sclerotic and violet



29 "Moth-eaten" scarring *folliculitis decalvans* in a Chinese, most probably following pyoderma. It should not be confused with the non-scarring "moth-eaten" secondary syphilitic alopecia.



30 Scarring alopecia following yaws papules of the scalp.
(Aars–Curaçao)

therapy. They are known as amoebid (CASTEX, TOURAINE, DUPERRAT) or *para-amoebiasis* (ROLLIER, MAURY, MÉRET in Maroc Méd. 1950). Not only amoebic dysentery is of interest for the dermatologist but also bacillary dysentery, since its FLEXNER and SHIGA strains may cause the *oculo-urethro-articular syndrome* with non bacterial pyuria, REITER's urethritis, bilateral conjunctivitis, polyarthritis, diarrhoea and probably pustules and skin lesions similar to those of lupus erythematosus. But who says that these symptoms do not originate from an old gonorrhoea in which cocci cannot usually be found? General adenitis has been described in these cases, but when present one should beware of overlooking secondary syphilis. MAKAR BEY in the Journal of the Egyptian Medical Association (1948) described a case of ulcerating cauliflower like *bilharzia polyposis* at the anus and on the thigh. Granulomata near the anus, therefore, should be carefully examined; one should also bear in mind the possibility of an atypical syphilitic primary lesion and/or condylomata lata or condylomata acuminata.

Angiomata are met with regularly in the tropics. Naevus flammeus in the neck is found less often among the autochthonous population than among whites, a fact which may perhaps also be attributed to the former's dark complexion. In Surinam, naevi and angiomata (which are not red but black) are called "lust" (*i.e.* "desire, longing") because they are attributed to the mother's longing for some fruit or other food during pregnancy.

In this connection we may also point to the naevus Unnae in the neck, which is found so often in Europe. Broadly speaking, when a prisoner of war I found this spot in 50 % of Europeans, 25   of half-castes and 33   of Australians.

Anthrax infection may cause one or a multitude of vesicles with a necrotic centre on an oedematous base going on to ulceration. The lesions may appear on any part of the skin. Although general illness is rare in this form of the disease, some fatal cases have been reported. (COLE, Brit. Med. Journal 1951).

Aphthae are very frequent in the tropics, both in the mouth and on the genitals.[1] Whether aphthae are due to vitamin deficiency is not

[1] Not to be confused with syphilitic plaques muqueuses!

known for certain they may also occur in well-fed people. The term, however, embraces various diseases, which can be classified as follows: a. *tropical aphthosis* or *Ceylon sore mouth* or *tropical sprue* a term applied to moniliasis, which has probably supervened pellagra, this in its turn having often been caused by chronic malaria etc. b BEDNAR's *aphthosis* at the rear of the back of the hard palate in children. This form is said to be due to thumb-sucking but it is not impossible that it is identical with the afore mentioned Ceylon sore mouth



31 Alopecia caused by sickle cell anaemia.
(Cornbleet c.s.-Chicago)



32. Alopecia in lepromatous leprosy
(Aars-Caracas)

c. MICKULICZ's *aphthosis* or *periadenitis mucosa necrotica recurrens* a very painful aphthosis which may lead to small ulcers It heals spontaneously within a period of two weeks Relapses may occur It is perhaps identical with d. *Touraine's aphthosis* probably a septicaemic process e. *Aphthous fever* or *foot and mouth disease* This condition is an epidemic disease among cattle, but may rarely occur in humans revealing oral umbilicated blisters f *Onyalai* an acute febrile and often fatal disease, may reveal blisters on the mucous membranes, which easily burst, the erosions being taken for aphthae

g CARDARELLI's *aphthosis* or *aphthosis cachecticorum* or *aphthosis Riga* is probably identical with onyalai. Splenomegaly and hepatomegaly as well as hyperpigmentation of the skin have been reported. g BEHCET's *syndrome* consists of genital and oral aphthae and ulcers, uveitis, iridocyclitis and sometimes pustules on the skin, erythema nodosum and erythema multiforme. The cause is thought to be a virus (BEHCET) or the bacillus crassus and it is said that smallpox vaccine may have a healing effect.

Oral lesions which may erroneously be diagnosed aphthosis are herpes, secondary syphilis and lichen planus of the mucous mem-



33 Moniliasis of the oesophagus.
(*Lignac-Leyden*)

branes, as well as actinic cheilitis in individuals sensitive to the sun. *Angular stomatitis* or *perlèche* may be due to vitamin-B_2 deficiency, yaws or congenital syphilis. (See njovera)

Artefactitious dermatoses are found both in the tropics and in Europe. One particular form is that which is not caused by hysteria but for beauty reasons, or as a quack treatment of some complaint. Among the former are the multiple small cheloids tattooed on the faces of Negroes and Maoris; the latter include the *kerab, kerik* or *adjat*, the treatment consisting of the production of multiple haemorrhagic spots by rubbing the skin with a red hot coin, for preference on the neck or on the forehead. The operation, which is called either "ouroudng" (Soendanese) or "pidgiting" (Javanese) is usually performed by the *dukun* or *sibasbe*, i.e. the medicine man or some member of the family. In some cases the purpura is combined with linear dermatitis, due to

after treatment with djeroek nipis (citrus) or quicklime, which may or may not be followed by cicatrization.

✓ A very interesting form of white magic should be mentioned here. This consists of piercing small golden needles into the skin, in order to prevent pain and disease, a practice amongst the Chinese. The lesions are minute as a matter of fact, but one may see an odd pustule sequestrating gold(!) many weeks afterwards and at a place where the





34 Artefact called "keroh" in the neck of a J a Chinaman and on the forehead of an Eurasian woman consisting of haemorrhages from scratching with or application of a hot coin as a treatment for sore throat and headache. (A primitive form of autohaemotherapy and perhaps a "forerunner" of ACTH treatment[1])

patient denies having done something" because the needles may move to quite a great distance Usually the needles remain under the skin without any reaction, being only accidentally discovered by X ray examination for one or other reason.

✓ The term *shook yang*, or *koro* stands for the superstition that the penis may shrivel up or suddenly "shoot back" into the abdomen, for which reason the males of certain tribes stick a bamboo pin or some animal s tooth through the glans penis as a safeguard against such an emergency

Simple tattooing, too is very frequent in the tropics The coloured skin may easily react with keloidous. The artificial keloidosis for

SAUER considers the effect of autohaemotherapy to be due to the stimulation of the adrenal cortex (J Inv Derm. 1951).

keloid tattoo however is provoked by smearing coal and various plant juices into the scarifications. Keloid tattoo is a primitive art indicating important facts of life. Tattoo along the nostrils indicates the "way of tears" and by this the first sorrow, tattoo around the navel is usually made after the first sexual intercourse, tattoo of or near the genitals may prevent the devil entering, etc. With tattooing we may also class the colours which the Hindustani apply to the



35 Bromoderma can be taken for yaws. *(Simons, Leyden)*

forehead as a temporary decoration, as well as the staining of the skin with kusuwe (the red fruit of Bixa orellana) by the red Indians—to which habit, in effect, they owe their epithet "Redskins". We also think in this connection of the red mouths of Indonesian women, caused by chewing sirih (see p. 131) and the use of "whitening" applications (*obat whiter* among the Japanese army of occupation). Finally I would mention the existence of certain cases of circumcision performed as an equivalent of tattooing (SIMONS, Dermatologica 1948, 2).

Atrophies. Not a great deal is known so far about *atrophies*. Physio-



36 This is North American blastomycosis.
(Goldman-Cincinnati)



37 And this is bromoderma.
(Fasal-San Francisco)

Both lesions are "framboesiform" and can therefore be taken for yaws. Framboesiform means "*naked*" or "*moist vegetations*" because the corneal layer is absent in contrast to what is seen in *papillomatous vegetations* with a corneal layer and in *verrucous vegetations* where the corneal layer is thickened



38 Leishmaniasis vegetative lesion.



39 The essential framboesiform lesion is the primary and secundary lesion in yaws.

Tw. more framboesiform or erosive vegetati lesions.

logical atrophy" stria gravidarum, is found also in the tropics. The tight belt (gurita) which Indonesian women wear after confinement does not prevent the appearance of the striae (REMMELTS). They may moreover appear apart from pregnancy and even in the male, due to



40 Boeck's disease in a Negress.
(Carol-Amsterdam)

hormonal influences. An interesting point is that keloidosis does not seem to occur on striae atrophicae. This may probably be attributed to the fact that this atrophy is not a cicatricial atrophy (*cf* lupus erythematodes, senile skin, leprosy, acrodermatitis atrophicans and anetoderma), while the factor of (slight) secondary infection is also absent.

Besnier Boeck-Schaumann's disease may be found in the tropics IRGANG in the Archives of Dermatology and Syphilology (1947) stated that a generalized form of BOECK's sarcoid with bone disease may be found among Negroes and probably more frequently than among whites. Boeck's *sarcoid* may easily be confused with tuberculoid leprosy. Even histologically the disease picture of tuberculoid (*i.e.*



41 Erythematous form of sarcoidosis Boeck in a Dutch woman from Java, initially diagnosed as (tuberculoid) leprosy. There is no histological difference; clinically analgesia is present in leprosy.
(*Vrijman—The Hague*)

sarcoid) leprosy is hardly distinguishable from any other sarcoid, the main difference being the presence of analgesia in leprosy. (*Cf.* chapter 21 and RALPH SCULL, Med. Clin. of North America, Jan. 1949).

Botryomycoma occurs more frequently in the tropics than in Europe. In some cases the tumour may be the size of a marble and even larger. It is often seen on the sternum of women who hold their kabaya

together with a pin. The big, fancy safety pin sooner or later pricks the skin, and the continual rubbing of the pin over the wound would seem to be the beginning of botryomycoma.[1]

The name of botryomycoma is derived from the name of castration tumour in horses, on account of the cells, which resemble yeast cells. The term, therefore, is actually incorrect; better ones



42. Granuloma pendulum or botryomycoma on the inside of the lower lip.

are *granuloma pyogenicum*, *granuloma teleangiectaticum* or *granuloma pendulum*, although the tumour does not always hang on a "stalk". Another synonym, *granuloma framboesiforme* is, in respect of the tropics, definitely confusing. Botryomycoma is often mistaken for keloid.

Bromoderma again, may easily be confused with yaws.

Buboes in the groin may be caused by the smallest wounds on the feet, but also by syphilis, chancroid or lymphopathia venerea. The appearance of a "bubon mixte" is by no means rare. It renders diagnosis difficult. Especially interesting are the low placed buboes in filariasis Bancrofti, which, it appears, immunize the leg against elephantiasis.

[1] MULLER, Lecture during captivity as a prisoner of war. Bandung 1942.

Buerger's disease or thrombo-angitis obliterans causes painful ischaemia and gangrene It may also occur in the tropics where it should be distinguished from tropical ulcer leishmaniasis, leprosy *Raynaud's disease* and even sclerodactylia. The cause is still unknown, heavy cigarette smoking being mostly blamed.

Carcinomas of the skin are described under the tumours.

Cheilitis (at any rate "cheilite de rouge") (lipstick cheilitis) naturally does not occur among races that do not use lipstick. *Actino-cheilitis* is



43 Buerger's disease.
(*Prijs-Jogjakarta*)

fairly often met with in the tropics Many cases may possibly be *actino-pellagra cheilitis* as cheilosis (whether or not caused by undue exposure to the sun's rays) is known to appear in ariboflavinosis, characterized by scaly lesions on the lips. This affection is classed with the seborrhoeic state of pellagra (*q.v.*) and may well be identical with the psoriasis labialis of WILLAN (1808) and the *pityriasis des lèvres* of RAYER (1835) The author saw one serious case of *cheilophagia* and *cheilotillomania* in a Chinaman, in the course of which the lips had become raw This may have been a case of *raw lip* as described by RAT in 1914 in which the lower lip swells and ulcerates This affection, however, has no known cause and would seem to be curable with great difficulty

Cheiropompholyx also called dyshidrotic eczema, is often met with

in the tropics, where it can sometimes even be widespread and quite as resistant to treatment as in Europe.

One even speaks of *tropical pompholyx* when capable of universal diffusion, and supposed to be the result of epidermophytosis. Since,



44 Cheiropompholyx which is often regarded as epidermophy*tid* from dhobie itch. A universal diffusion is called tropical cheiropompholyx.
(Siemens–Leyden)

however almost every inhabitant of the tropics—also therefore, those with cheiropompholyx— has, at some time or other, had either an athlete's- Singapore- Hongkong foot or "bathroom eczema" it is hard to decide whether this dyshidrosis is in fact, an epidermo-

phy*tid*. The condition, which, despite the name, has no connection with the sweat glands may last for a long time during which it may reveal periods of "cure" In its chronic desquamative or lichenification stage it may again become active, showing new vesicles the contents of which may contain pyococci or fungi.

At this point we may also call attention to *dermatitis excsiccans*



45 Condylomata acuminata of the eyes may occur in their absence on the genitals.

palmaris (" Formosa eczema ") a rhagadiform, tylotic eczema of the finger tips which may lead to contracture of the affected fingers. In some cases the toes are also affected The affection occurs mostly in women and it is not certain that it is not identical with HAXTHAUSEN's hyperkeratosis palmoplantaris climacterii

Chilblains I found only two cases reported by ARIAS in Costa Rica (Rev med. Costa Rica 1951)

Chloasma is decribed under photo-dermatitis and pigmentation.

Chromhidrosis a rare disease, may occur anywhere, also in the tropics where, among others, LAMPE (Jakarta 1941) observed a case.

Calloid milia are found in the tropics at least as frequently as in colder regions

Condylomata acuminata and *-lata* are often met with in the tropics The former are found far less often in circumcised than in uncircumcised men this also applies to balanitis

Creeping disease is of regular occurrence. It is sometimes confused with linear dermatoses (even with herpes zoster), which linear derma

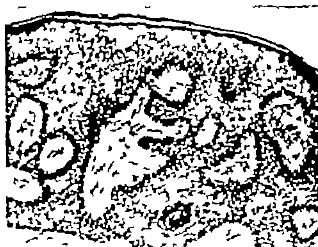




46 Dermatosis papulosa nigra.
(Oor G Costa-Belo Horizonte) *(Fasal-San Francisco)*

toses are caused by among other things, insects which creep over the skin and leave their trace in the form of some secretion or other "*Cockroach dermatitis*" is one of these affections. In some cases there is oedema of the eyelids this is also attributed to the cockroach, which is supposed to prey on any ocular secretion—at any rate if it is true that *this* form of QUINCKE's (?) oedema, which is relatively frequent in the tropics but less so in Europe, is caused by the cockroach. It is interesting to note that this insect is blamed for the affection in Surinam as well as in Indonesia (*kakkalakka bitin* or *-busse* i.e. cockroach bite or -kiss) (*vide* also under urticaria).

Defluvium capillorum The contention that "loss of hair" is less general in the tropics than in other regions is, to my mind confusing I regard *calvities* in the male as a phenomenon similar to losing one's milk teeth. In my view a man gets his own racial form of hair growth by about his 20th or 30th year of age. Owing to miscegenation, however the aboriginal form can no longer be traced but that is no reason to confuse a pathological condition with a sexual or racial characteristic. VANDBREUSEGHEM reported in the



47 Dermatosis papulosa nigra.
(Fasal-Sen F andten)

Belgian tropical Annales of 1947 a case of *keatrichia* in a Congolese This reminds me of the blue eyes among some natives of the Polynesian island Pitcairn where, however Captain BLIGH's sailors settled after the mutiny on his ship The Bounty in 1791

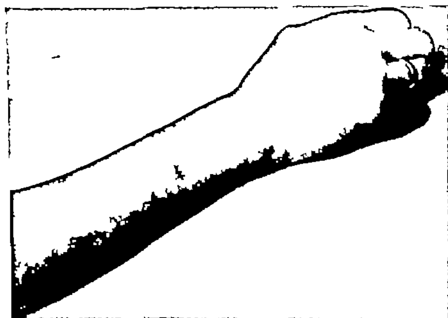
In Trinidad I saw a woman of probably not pure India-descent with blue eyes, in Aruba I saw a young man, Red Indian with blue eyes and in Indonesia Eurasians with grey eyes are often met with.

Diphtheria of the skin with regard to cutaneous diphtheria we refer the reader to the chapter on paedodermatological observations in the

tropics, to the chapter dealing with tropical ulcer as well as that on cutaneous diphtheria.

Dermatitis herpetiformis (DUHRING's disease) The author observed one case (a Dutchman in Indonesia), and another (a Greek in the island of Aruba). Neither of these two cases was any milder—nor for that matter graver—than those generally observed in Europe.

Dermatosis papulosa nigra consists of minute black papules sym-



48 Leukoderma due to toxicoderma from aspirin in a Dutch woman in Java.

metrically spread on the face. It is most often seen in the Negro. The condition is benign and histology reveals acanthosis and still more hyperpigmentation. The papules probably originate from the sebaceous glands. (MICHAEL and SCALE, Arch. of Dermat. and Syph. 1939).

Dermatographism is very frequent in the tropics. The same applies to urticaria.

Drug eruptions are found especially after the application of iodoform

and of "obat macham" (*i.e.* tiger balsam)—both of which are very popular— and after the internal use of sulphonamides, penicillin-tablets, mepacrine and quinine. The external application of sulpha drugs may also set up the well-known reactions. *Lichenoid atabrine dermatitis* (the tropical lichen planus syndrome) which may appear as late as two months after the ingestion of atabrine, may assume a reddish-yellow "pre mycotic" [1] aspect, due to the simultaneous yellow discoloration of the skin caused by atabrine. A more dangerous disease is *exfoliative atabrin dermatitis* (and *-hepatitis*), which may be fatal (AGRESS in J. A.M.A. 1946). *Atabrin-* or *quinacrine dermatitis* which, therefore, must be differentiated into the usually described lichenoid and the universal exfoliative form, is sometimes coupled with toxic alopecia, keratitis and conjunctivitis. The affected parts sometimes show irregularly shaped pigmented or depigmented patches which, however should not be confused with tinea flava. Much has been published in the Anglo-American literature on the subject of *atabrinoderma*, often under the name of *atypical lichen planus*. BUTLER (Arch. of Dermat. and Syph. 1947) studied over 200 cases of which the severer forms showed generalized adenitis and alopecia areata in addition. The oral mucosa was frequently involved, the genitals sometimes showed lesions like those of condylomata lata and the nails were commonly thickened.

Neurological and intestinal as well as haematological changes were probably due the accompanying vitamin deficiency. GINSBERGER and SHALLENBERGER (J. A. M. A. 1946) found a distinct greenish-yellow fluorescence of the nails in Wood's light.

FINDLAY in the Tropical Diseases Bulletin of 1947 (Vol. 44 No. 9) gave a detailed survey under the title "The toxicity of mepacrine in man"[2] (Vide also the remark on psoriasis following the use of quinine p. 117). *Arsenicoderma* should receive some extra attention, since arsenic poisoning is often carried out as an attempted murder and is therefore usually obscure. It can easily be taken for pellagra, because of various similar features and accompanying signs, *e.g.* diarrhoea, general weakness, erythemata, pigmentation and hyperkeratosis. The

[1] *i.e.* that of the so-called pre mycotic stage of mycosis fungoides.
[2] See [illegible] and Rubin in the Journ. of investigative dermat. 1950 and [illegible] same journal, 1951

pigmentation may surround the neck similar to CASAL's pigment collar in pellagra, for which reason it is termed casaloid[1] Chronic arsenical poisoning may cause a transverse striate leuconychia, the distance of which from the nailfold may be valuable in determining the beginning of the poisoning because the nails grow three millimeters per month The main condition, however to discover the arsenical poisoning is to consider it in all pigmentations and diarrhoea



49 Sub-tropical lichen planus.
(Sagher Jerusalem)

of unknown cause. Arsenicoderma due to inorganic arsenic, which is meant here, differs from that caused by organic arsenicals, *e g* neoarsphenamine dermatitis which, however may result (particularly in coloured patients) in ugly pigmentation, and loss of hair and nails. Arsenical dermatitis from neoarsphenamine, of course, is also found in the tropics, erythrodermatically or in an eczematid form and as a lichenoid eruption. Two cases are worth describing briefly

[1] R. D G Ph. Simons *Arsenicoderma* Thesis Univ of Leyden 1937

The first case was an arsenical dermatitis in a man who had been treated with neoarsphenamine for lichen planus. The physician took the incipient dermatitis for the spreading of the lichen planus and continued the disastrous therapy with the result that the patient died.

The second case was one of an arsenical dermatitis in a Dutch woman, who had received neoarsphenamine for a tylotic eczema which was diagnosed as yaws.

Neither the *direct biotropistic Jarisch-Herxheimer reaction* in the treat



50. Dermatitis due to the rengha-plant
(Fasal—San Francisco)

ment of syphilis nor the "*lepra reaction*" in the treatment of leprosy is a toxicoderma. Neither are the "ninth day erythema" (which is often not recognized as such) and jaundice classed as genuine toxicoderma since these two belong to the so-called indirect biotropisms.

Eczema. Apart from certain occupational eczemas, which are specific to the tropics on account of particular trades (*e.g.* dermatitis caused by the lacquer of Rhus vernicifera, by jute, *derris* (called neku in

Surinam), by manga, vanilla, pyrethrum, teak wood (Tectona grandis) palisander by the sap of the *possentri* (*i.e.* poison tree, Hura crepitans) and various other Rhus genera—vide also pemphigus), there is relatively little qualitative difference between the tropics and Europe or the States Eczemas in all forms—especially intertriginous eczemas—are found both in the hot coastal regions and in the mountain districts maybe less frequently than in Europe, but none the less fairly regularly The intertriginous eczemas are often secondarily infected by fungi In this connection one should bear in mind the many confusions of shoe-lining eczema and epidermophytosis.

Jungle dermatitis ("dermatites forestières") is eczema which is caused by certain plants, particularly anacardiaceae and euphorbiaceae, a few of which we have already mentioned. The most notorious anacardiaceae are, surely the *renghas* (Gluta renghas redwood and resin) and the kemang (Mangifera caesio latex) the most dangerous euphorbiacea is no doubt Hippomana Manchinella, better known by the name of *Bringamosa* (= the quarrelsome woman) of the Antilles In Indonesia, some plant names have the suffix *gattel* meaning "itch"—a significant idiom— as, for instance, the widely known *daon*- and *katjang gattel* (Mucuna pruriens) with its hairy seeds and leaves that cause severe itching We find something similar in Surinam the *tetremenan is* the Red Indian name for itching wood a name used for a species of timber better known by the name of *mam* the sawdust of which also causes itching KATSER further mentions the *kaju buta buta* (Excoecaria agallocha) of Java, which causes little itching but whose sap may set up severe conjunctivitis and even cause blindness (*arbre aveuglant i.e.* the "blinding tree") Another jungle tree the sap of which may cause dermatitis is the *upas tree* (Antiaris toxicaria) called *pohon upo* This sap was used by the Sakais, the Malay aborigines, to poison the darts of their blowpipes (FASAL in the Arch. of Dermat. and Syph. 1945) *(See also in the chapter dealing with allergy)*

As we shall see further on, the "dermatites forestières" (jungle dermatitis) which are contact dermatitis, or at any rate, start as such, should be distinguished from allergic plant eczemas which are not preceded by a contact dermatitis, and from phyto-photo-dermatoses There is not a great difference between jungle rot and an infectious "dermatite forestière" The former is also synonymous with infectious

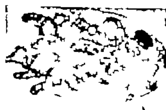
eczematoid dermatitis (dermo-épidermite microbienne), in which there are hardly any pustules—if at all only an oedematous swollen skin with a few pointed crusts around a pyogenic process, *e.g.*, on the



51. Seabather's eruption (not to be confused with swimmer's itch or jelly fish dermatitis)

(Saint-Miami)

ear or the skin of the face, around an otitis media or interna. One might call this a perifocal or circumfocal infection or reaction. Certain



52. Copra itch is not a plant eczema but an epizoonotic pruritus from the caroglyphus ovatus.

(I an Schem en–Rotterdam)

sharp grasses often cause n dermatitis but scarifications which may be infected secondarily

Sett or *Sadd dermatitis* is caused by water-grasses the most important

of which is Panicum pyramidale (Egypt) *Seabather's eruption* is a papular pruritic eruption (Florida coast, Bahama islands) which is probably due to some microscopic marine organisms (SAMS Arch. of Dermat. and Syph. 1949) The name should not be confused with



53. Prurigo nodularis of the extensor surfaces of the thighs is often due to bed bugs, living in rotten chairs. *It should be distinguished from rotten lacquer dermatitis and it should* be borne in mind that the "rotten louse" often turns out to be the bed bug

swimmer's itch or schistosome dermatitis nor with jelly fish dermatitis (*q.v.*)

A dermatitis which, though not phytogenous, bears the name of *copra itch*, is an epizoonosis in workers producing copra from coconuts It is an itching, urticarial, vesicular or pustular affection, actually caused by Tyroglyphus longior a genus of acarids which, in contrast to Sarcops scabiei, does not bore into the skin, and is only found on

the skin immediately after contact with the copra. A similar phenomenon may be observed on tea plantations through contact with Rhizoglyphus parasiticus.

Pineapple itch or *pineapple estate pyosis* too, should perhaps be attributed primarily to an acarus.

To the same group belongs the zoonosis caused by the patata louse, described further on in this chapter.

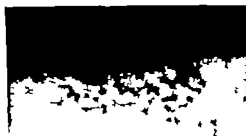
Rottan dermatitis is most frequently found to occur on the lower



54. Furunculoid bed bug bite lesions from sitting in a rottan chair which proved to be infested by bed bugs.

arms and back of the thighs. It is characterized by urticaria, papules and sometimes also by prurigo and is caused by insects living in the twisted curls of cane chairs. In most cases the "rottan louse" turns out to be the common bed bug. As prisoners of war in the Japanese camps we used to notice that the bug comes out at night and may travel some dozens of yards to find its prey. The moment the light goes on, however, the bed bug scampers into the smallest hiding places such as folds in the mosquito-net, niches, books, etc. For this reason one cannot always give prima facie credence to a patient's statement that he has no bugs.

In this connection we may mention the appearance of a linear bullous eczema on the calves of tram passengers which occurred



55 Collector's or Swimmer's Itch. Schistosome-dermatitis.
(Orig. G. Castro-Belo Horizonte)



56. Elephantiasis due to *filariasis Bancrofti*.
(I. van de Poll-Amsterdam)

epidemically in Dundee and in Amsterdam, and which turned out to be caused by bugs dwelling in the crevices of the tram-seats.

Other itches already referred to are, *Bedouin's itch* (German measles,

prickly heat) *summer's itch* or *schistosome dermatitis*, *coolie itch* or *cavalot* or *ground itch* also known as *mazamorra*, *panighao*, *dew itch* or *swamp itch* on account of the penetration of the skin by the larvae of uncinaria; *dhobie itch* i.e. epidermophytosis in laundrymen, and "*marking ink dermatitis*" in those who use bhilawan oil of the semecarpus ana



57 Elephantiasis nostras due to recurrent erysipelas. Many cases of elephantiasis from filariasis Bancrofti become complicated by recurrent erysipelas, which may result in a combination of both forms.
(Orig. G. Caste-Bele Hartmann)

cardium; *grain itch* or *acaro dermatitis urticaroides* caused by the straw mite Pediculoides ventricosus; *Malabar itch* or superficial trichophytosis, and *Cuban* or *Philippine* itch for alastrim.

Epidemic dropsy also deserves mention at this point. This disease

which may show a strong resemblance to beri beri is however caused by curry or chicken food vitiated by the presence of the seed of Argemone mexicana The dermal phenomena are roseolae, telangiectasiae purpura and slightly bleeding papules. Other symptoms are dyspnoea, anaemia and pain in the bones and muscles.

Flit dermatitis is sometimes seen, especially in women who spray the legs with "flit" Jointly with JENNY SIMONS JANTZEN, the present



58 A non-filarial case of elephantiasis in a Negro probably due to cutaneous leishmaniasis.

author published a detailed account of this affection. See Yearbook of Dermatology 1940 It became evident that the name flit-dermatitis is also applied to dermatitis from other mosquiticides and that the most harmful insecticides from their contents are oleum terebinthinae, oleum citri and perhaps also flores pyrethri (?)

In large oil refineries one often comes across dermatoses caused by petrol derivatives and plastic materials

In *sugar refineries* one frequently finds sugar nails" or sugar paronychia these however are usually fungus diseases (*q.v.*).

"Sugar cane ear" kepai ko in the Hawaian isles caused by sugar cane being carried on the shoulder and rubbing against the ear is fortunately a thing of the past, thanks to modern means of transport.



59 Slight elephantiasis and mossy foot in chromomycosis also though erroneously termed chromoblastomycosis because this fungous disease is not a true blastomycosis. (See also Fig 17 and volume II).
(Piers–Nairobi)

In *rubber factories* the soles of the feet of workers may be affected by acids used in the manufacturing process This may lead to confusion with keratoma sulcatum, which is said to be due to yaws

Soapdermatitis is often not recognized I have seen cases regarded plant

eczema, scabies and even as a papular rash fro
salves and particularly bathing with socalled
the dermatitis going on which may rese
lichenified eczema. The same is applicable t
balm, the panacea of South East Asia and
which are locally applied, as well as derm
ointments

Elephantiasis nostras due to chronic ery

60 Elephantiasis (Pantalon de
due to neurofibroma

seldom. *Elephantiasis graecorum* is found
arabum in filariasis Bancrofti (*q.v.*) Recklin
may also cause elephantiasis. *Pseudo ele*
Quincke's oedema. Here I want to refer
LOEWENTHAL's *lymphostatic verrucosis* which
ry foot from chromomycosis and which is
tion of elephantiasis in filariasis Bancrofti
the absence of fungous elements and
important to draw attention to the fac
cosis is also met with in regions where filar
Most probably the condition is a form of
again is usually attributed to recurrent

thema, resembling *erythema centrifugum circinatum* (or *erysipelas*), and on that account, also called *erysipeloid* was often observed in the P O W camps. It may be caused by the bite of *Ixodes ricinus* but it is also possible that it is an erythema multiforme, and not, as has sometimes been supposed, a form of pellagra (*vide* under pellagra).

Erythema nodosum also definitely occurs in the tropics (see index).

Erythema exudativum multiforme is found in the tropics but far less frequently than in Europe. The author once saw a markedly bullous form which reminded him of *pemphigus vulgaris* This *hydroa* responded



62. Elephantiasis vulvae from filariasis Bancrofti.

at once favourably to penicillin It relapsed a month later but disappeared again as promptly upon treatment with penicillin.

Erythema solare is, of course, very frequent (*vide* also erythema centrifugum, under pellagra).

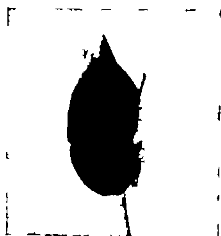
Erythema induratum (BAZIN s disease) is hardly ever if at all, met with in the tropics.

Roseolar erythema occurring in syphilis and typhoid fever is found relatively often. The former is sometimes attributed to poisoning by shrimps. The "*roseoles*" appear on the dark skin, instead of rose ("teint triste") brown, and soon become black, owing to haemosiderotic pigmentation.

Erythema pernio See *chilblains* page 60

Trans. Royal Soc Trop Med. 1948) A similar condition may also occur in filaria-elephantiasis and in my opinion it may be a sequel of any oedema JELLIFFE reported a case in tertiary yaws (Trop Med. and Hyg 1951)

Epidermolysis bullosa a rare dermatosis has been reported occasionally in the Negro JOSEPH and WITHERSPOON have recently described the dystrophic form in two sisters and the simple form in two brothers of another family (Arch of Dermat. and Syph 1951).



61 Pseudo-elephantiasis actually Quincke's oedema of the penis following betarsan therapy of filariasis Bancrofti.

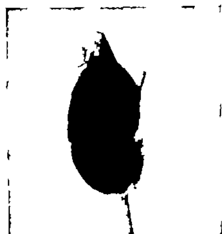
Erysipelas is often found in the tropics particularly as a complication of elephantiasis filariensis Conversely chronic erysipelas may cause elephantiasis or may promote its developing from filariasis LAMBILLON in the Annales de Soc. Belge de Med. Tropicale (1947) described a form of erysipelas occurring in a case of malaria, which was cured by mepacrine treatment.

Erysipeloid (BAKER–ROSENBACH's) is met with now and again, but is rarely brought to the skin specialist's notice. It is caused not only in preparing pig's flesh, but also in the preparation of shrimps or fish.

A mild, non-febrile, ribbon-shaped and sometimes migrant ery-

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thema, resembling *erythema centrifugum circinatum* (or *erysipelas*) and, on that account, also called *erysipeloid* was often observed in the P O W camps. It may be caused by the bite of *Ixodes ricinus* but it is also possible that it is an erythema multiforme, and not as has sometimes been supposed, a form of pellagra (*vide* under pellagra)

Erythema nodosum also definitely occurs in the tropics (see index).

Erythema exudativum multiforme is found in the tropics but far less frequently than in Europe. The author once saw a markedly bullous form which reminded him of *pemphigus vulgaris* This *hydroa* responded



62. Elephantiasis vulvae from filariasis Bancrofti.

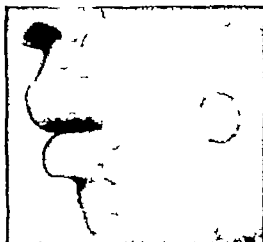
at once favourably to penicillin it relapsed a month later but disappeared again as promptly upon treatment with penicillin.

Erythema solare is, of course, very frequent (*vide* also erythema centrifugum, under pellagra).

Erythema induratum (BAZIN's disease) is hardly ever if at all, met with in the tropics.

Roseolar erythema occurring in syphilis and typhoid fever is found relatively often The former is sometimes attributed to poisoning by shrimps. The "roseoles" appear on the dark skin, instead of "rose" ("teint triste") brown, and soon become black, owing to haemosiderotic pigmentation.

Erythema pernio See *chilblains* page 60






63–66 [illegible] philis (see also left nostril), yaws, tuberculoid leprosy [illegible] pical lichen planus. See footnote 2 page 10

(Prof. [illegible] Co[illegible]ta–Belo Horizonte, Kraldhge–Groningen and Sagher–Jerusalem)



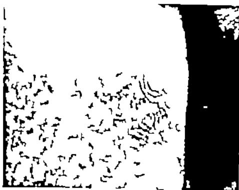
67 Ringworm or tinea corporis.
(Osw. G. Costa–Belo Horizonte)



68 Not ringworm but secondary syphilis of the scrotal skin.
(Siemens–Leyden)



69 Cutaneous leishmaniasis.
(S[illegible]–Amsterdam)



70 Tinea imbricata of the right thigh.
(Area Leão–Rio de Janeiro)

67–70 Four more circinate dermatoses: tinea corporis, pseudo-ringworm from secondary syphilis, tinea imbricata with watered silk appearance of concentric scale, and an atypical form and typical localization of cutaneous leishmaniasis, often called "tropical lupus vulgaris" because it may even reveal the "apple jelly" phenomenon of true lupus vulgaris.

Erythroderma as well as being caused by arsenicals is also found occasionally to be the result of MANSON's pyosis which we will describe later in some detail. The author once came across a psoriasiform dermatosis caused by quinine, which rapidly spread erythrodermatically (See also psoriasis)

Folliculitis barbae is infrequent in the tropics because the natives are mostly beardless in addition to which what little beard they may have



71 A peculiar condition in the Negro is *scarring pseudofolliculitis* (PINKUS) due to shaved hairs growing back into the skin of the cheeks and sides of the neck It is identical with pili incarnati and traumatic folliculitis, but it should be distinguished from true folliculitis barbae.

they do not shave but depilate. An affection often seen is *folliculitis decalvans capitis* in Chinese children, which may lead to multiple atrophic spots which should not be confused with *syphilitic alopecia* or with alopecia areata. A peculiar condition is the scarring pseudo-folliculitis shown in Fig. 71

Fungous diseases occur in all their forms in the tropics, and indeed, in even greater variety than in Europe Epidermophytosis has many tropical names such as Singapore foot although the majority of these feet or clinical "epidermophytoses" are not due to the epidermophyt n tur… c lled fl ccosum.

There is much confusion in the terminology of the blastomycoses, but all this will be discussed in volume II

Gangosa (rhinopharyngitis mutilans) is usually attributed to yaws but the author saw in Surinam, (in a district where yaws is frequent, but where espundia is not unknown either) a case of "burnt-out" gangosa, the aetiology of which it was no longer possible to determine.

Gangrene is far from rare, and may have the same causes as in Europe. CHRISTOPHER's *Textbook of Surgery* contains a description of a pyo-



72. Will this case of late yaws or syphilis in a Javanese develop into gangosa or goundou?
(v. d. der Zijl—The Hague)

derma which may rapidly lead to gangrene. It occurred once or twice in the P O W camp in Sumatra, and is described in more detail further on (under pyoderma) (*Vide* also noma ainhum, granuloma gangraenescens)

Scrotal and perineal gangrene also called "gangrène foudroyante des organes genitaux" (DARIER) tropical pudendal phagedena (ASH and SPITZ) may complicate bacillary dysentery (CONNOR) or malaria (STRONG) It may also be due to rupture of the urethra, causing urine to infiltrate into the tissues, to phagedaena from chancroid

or according to VANBREUSEGHEM to a virus, which becomes phagedaenic when in symbiosis with "various microbes"

Granuloma annulare can occur in the tropics but should not be



73 Gangosa from yaws, espundia or a harelip? I met this man at the railway in a place where yaws as well as muco-cutaneous leishmaniasis are common.



74 Rhinopharyngitis mutilans or gangosa in an initial stage. (See also Fig 19 102 and 237)
(Elshout-Bendert)



75 Scrotal gangraene.
(Vanbreuseghem–Antwerp)

confused with other circinate lesions of syphilis, yaws, leprosy or leishmaniasis. (See Fig 100)

Granuloma gangraenescens is a rare condition of unknown aetiology It rapidly results in a horrible destruction of the face and facial







76–78. Granuloma gangraenescens in a Javanese The photographs were taken at Jan. 3rd Jan. 18th and at March 27th (fatal end) no visceral lesions.

(Prigo–Jogjakarta)

bones and invariably leads to death. DENNIE and HAMILTON attributed a case to a pathogenic form of Spirochaeta microdentium (Arch. of Dermat. 1940) and JONKHOFF to mycosis fungoides (personal communication) It is probably not identical with noma





79–80 And this c se f granuloma gangraenescens in a Dutch woman which alu ded fatally within one year The condition was regarded as a f rm of mycosis f ngoides because of the histology of he ght ro old granuloma on her breast.
(Jeakhoff–Groningen)



81–82. Universal ichthyosis in a Sino-European girl from Java.



83. Keloidosis following tropical acne and pseudo-folliculitis barbae in the Negro. (See Fig. 71)

which has been described further on and therapy is unknown. Perhaps antibiotics may prove valuable.

The various forms of *herpes* including *herpes zoster* are regularly met with in the tropics In one of the P O W barracks in Sumatra out of a group of six men, two had varicella, and two herpes zoster the other two remained healthy It is interesting to note the Papie



84 Keloids in circinate tertiary syphilis of a Javanese.
(Van der Zijl-The Hague)

mento (i e Antilles dialect) name for herpes, i.e. *kalibrie*" (= humming bird) In a comparative investigation into the incidence of herpes zoster in Western Europe and Indonesia, I found that the frequency of zoster in all dermatological cases was almost ½ % For the northern hemisphere it appeared that zoster occurs least frequently in winter but in Java it is least seen in the wet monsoon corresponding

to summer of the southern hemisphere (i.e. January until April)[1]

Hidradenitis is more frequent in the tropics than in Europe, both among men and among white women—the latter because of the prevalent habit of shaving the armpits.

Hidrocystomata are quite frequently met with in the tropics, where they are as often as elsewhere confused with milia, colloid milia and even miliaria. Hidrocystoma represents a chronic non-inflammatory cyst of the sweat gland. *Sudamina* have a more acute and temporary character. *Milia* or white heads are minute non-inflammatory retention cysts of the pilosebaceous follicles. *Colloid milia* are yellowish translucent nodules corresponding to the presence of colloid masses underneath the epidermis independent of the appendages of the skin. *Miliaria crystallina* are synonymous with sudamina. When they are inflammatory they are called *miliaria rubra* or prickly heat. When the prickly heat affects the face, it may have a papular appearance, for which reason it is also called *lichen tropicus*. Oral administration of



85 Keloid on the breast following tattoo which has become secondarily infected by alastrim; in the armpit following hidradenitis and at the ears (from eardrops?).
(Vanbreuseghem—Antwerp)

[1] R. D. G. Ph. Simons, Dermatologica, 1951

atropine sulphate causes a hydrocystoma to disappear within some days. Intake of pilocarpine hydrochloride causes them to recur (DOSTROVSKY-SAGHER test).

Ichthyosis occurs among the coloured races. It should not be confused with tinea imbricata universalis and, definitely not, with a slight chronic soap dermatitis which, when not recognized as such, is sometimes "treated" with coal tar or mercuric soap. Crazy pavement dermatitis from vitamin deficiency (also when occurring in leprosy) may be taken for ichthyosis.



86. K[illegible] m plantarum is often said to be due to yaws, but cases [illegible] are known. The condition may be unilateral. (Aars-Caraçao)

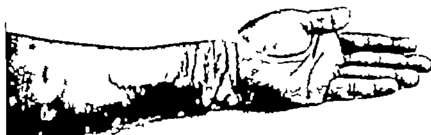
Juxta-articular nodes. See under Nodosités juxta articulaires.

Keloid or keloid formations are of frequent occurrence (see p. 51).

Keratoma plantare sulcatum which is quite often seen in barefooted adults in the tropics [illegible] usually said to be due to tertiary yaws, but its

cause is still obscure. The soles of the feet are thickened and pitted. In some cases the affection is unilateral. I have seen similar lesions in men working in the factories of rubber plantations caused by the lactic acid which is always copiously spilt on the factory floors.

Leptospira infections During the last 20 years it has become known that there exist numerous species of Leptospirae, differing in serological structure and often also epidemiologically (*i.e.* transmitted by different vectors) although differing only slightly as a rule, in the clinical features they cause. WEIL's disease is marked by fever, often in two phases, violent headache and pain in the muscles especially those of the calves and the back. The patient may die of hepatargia or uraemia, while meningeal phenomena (meningitis serosa) are not



87 Kobner's phenomenon (*i.e.* a linear eruption following a scratch) of lichen ruber in the Negro

(*Aars-Caraçao*)

unusual. The patient's appearance is characterized by a red, swollen face and congestion of the bulbar and palpebral conjunctivae. Jaundice is present in about 10 per cent. of cases. The skin is universally erythematous. In about 10 per cent of the cases there is a rash, macular and roseolar sometimes papular in other cases it may be petechial, resembling a scarlet fever eruption. The rash usually appears between the 3rd and 5th day and does not last long – only a few days or even hours. The mucosa of the mouth and pharynx is also often reddened. Herpes labialis is rarely seen. In gravely affected patients haemorrhages of the internal organs in the skin and conjunctiva and suggillation of the oral mucosa may occur. It is



88 Hidrocystomata.
(Sagher–Jerusalem)



89 Hidrocystoma
(Sagher–Jerusalem)

highly probable that the fundamental cause of all this is a general capillary toxicosis.

A slightly different syndrome is that of *„mud fever"* or *„swamp fever"* *(leptospirosis grippo-typhosa)* in which a rash resembling measles is often seen. Data concerning the frequence of the rash in other leptospirose are, as yet, insufficient thus the percentage given for leptos-



90 Eau de cologne dermatitis in a Javanese girl, which was not followed by pigmentation.

pirosis canicola varies from 0 to 20% as between the different statistics. (Personal communication by Prof W KOUWENAAR Amsterdam)

Lichen planus The remarks we made concerning psoriasis also apply to *lichen ruber* or *lichen planus* The writer once saw a Negro with wide spread lichen ruber (physician AARS), in which the Wickham s striae were so distinct that the man looked as if he had been sprinkled over with silver. (See also drug eruptions.)

A communication by LENNHOFF in the Acta Dermato-venereologica (1948) deserves mention in this connection the author reports the discovery of spirochaetae in the lesions of lichen ruber

Light or photo-dermatoses are frequently met with—they should not be confused with dermatoses forestières, already mentioned, nor jungle dermatitis from which prickly heat must be distinguished. Ultra-violet rays—which, by the way may also give rise to bullae—

are capable of causing skin affections either directly or following previous sensitization. Sensitization may be caused by certain "photo-sensitizing" substances which make the skin sensitive to light, either by external application (sulphanilamide-ointment, oil of bergamot), or with more general effect, by internal use (*e.g.* sulphonamides, acridine derivatives, etc.). According to KUSKE the most important sensitizing agent, which is present in different plants and herbs, is



21. Berloque dermatitis from eau de cologne. The arrow indicates the part of the skin protected by a ring.

furocoumarine which is not an allergen as such, but only modifies the photo-resistance of the skin. This causes the appearance of the irregularly shaped erythematous or erythemato-bullous and slightly pigmented lesions in *phyto-photo-dermatoses* (also called *dermatitis pratensis*, *meadow-dermatitis*, OPPENHEIM's *disease* or *photo-dermatitis actino-calorique chlorophyllienne* (KITCHEVATZ), better "*furocoumarinum*" (KUSKE). The pastinaca plant (white carrot or parsnip) which, in Europe, grows in large quantities along the dykes and is one of the worst offenders

in causing this affection, does not grow wild in Indonesia there, instead of the Umbelliferes it is especially the Rutacea, including the Citrus, that play the biggest part and in these cases it would be incorrect to speak of a *weide*-dermatitis (*Weide* means meadow") Citrus dermatitis, or discoloration, is also known by the name of *berloque* or *pendant-dermatitis* owing to its form. It occurs in those who peel the Citrus fruit with their teeth, causing the juice to run down the chin and on to the hands or who use citronella oil to ward off mosquitoes or who cool their face by moistening it with eau de cologne containing



92. Bullous fig dermatitis.
(Berlin-Tel Aviv)

bergamot oil from the citrus plant (see Fig 90 and p. 91). Other „dermatogenous species are the Moraceae (e g the fig plant), the Ranunculaceae, the Cruciferes and the Rosaceae, including agrimony All these plants are also found in the tropics, the Rosaceae at over 5000 feet above sea level. It is interesting to note that creek water sweat droplets and particularly sea water (e salt, seaweed) act as photo-sensitizing agents (Fig 96), and may probably be reckoned

among the causes of tropical chloasma (*vide* also p 111 Figs 113 and 114) A clear distinction should therefore be made between (a) pure *dermatites forestières* in which light plays no part, and which are either contact dermatoses or start as such (b) those *allergic eczemas* (*e g*, caused by primula [1] which are not preceded by primary dermatitis (c) *phyto-photo-dermatoses* (d) *photo-balneo* (sea water) *dermatoses* and



93 Dermatitis pratensis a phyto-photodermatosis. (*Simons Leyden*)



94 Blister not from any insect, but belonging to a phyto-photo dermatosis.

(e) *epizoonoses* which are acquired in brushwood and undergrowth. For the sake of completeness we also mention *coup de lumière acridinique* or *sulphanilamidique* which, instead of an irregular shape, usually shows an even discolouration of the parts that were exposed

[1] Out of the m y pl   which m y cause "weide" dermatitis, *Achillea millefolium* is indigenous I de n

to light (*vide* also pp. 99 and 100) A notice by SONCK about hyper sensitivity to light in lymphopathia venera appears in the relevant chapter.

The simplest form of "photo-dermatosis" is, surely postponed solar erythema followed by pigmentation. As a rule there is a certain "tolerance" for which reason the irradiation should be successively prolonged to obtain the same effect but cases are also known where



95 Eruption of varicella particularly on parts having been exposed to the sun.

an individual reacts suddenly with sunstroke (better called *coup de lumière* than "coup de soleil") (DARIER) by a violent erythema, to the irradiation which had previously been tolerated quite well.

Despite many theories, such as those of photo-allergy and photo-toxicoderma, this problem has not yet been satisfactorily solved. All we know is that porphyrins may increase sensitivity to light, although cases of porphyrinaemia are known where the patient was not hyper sensitive to light. (*Vide* also under pellagra, and p 113)

A *Light as the essential noxious agent*	Actino-dermatoses
1 hydroa vacciniforme BAZIN	(DARIER)
2 summer prurigo HUTCHINSON	or
3 urticaria solaris WARD	Lucites or helio-dermites
4 xeroderma pigmentosum KAPOSI	(GOUGEROT)



98. Intense erythematous, papular and urticarial "sun rash" in a woman who has become photosensitive because of lymphopathia venerea.
(Sauck-Helmold)

B *Light as a contributory noxious agent*

1 pellagra

2 lupus erythematosus

3 other dermatoses, including erythema multiforme

C *Light as complicating noxious agent*

E.g., in smallpox, pigmentary anomalies etc.

SONCK further remarks that it is not impossible that certain cases of summer prurigo must be attributed to the virus of lymphopathia venerea (*q.v.*) SELLEI in the Archiv für Dermatologie und Syphilis (1930), gave the following classification

1 *Prurigo solaris* with prurigo and urticaria, and *eczema solare* with eczematous phenomena. Both these affections are seasonal diseases which cannot be caused by ultra violet rays (*vide* also p 100)

2 *Urticaria solaris* which does not depend on the time of the year but appears whenever the light shines on the skin (allergic reaction or actino-anaphylactosis (JAUSION[1])



99 Lupus tumidus in a Negress. (*Peers–Nairobi*)



100. Granuloma annulare" from late secondary syphilis in the Negro (*Aars–Curaçao*)

In 1948, POLANO in the Nederlands Tijdschrift voor Geneeskunde ("Netherlands Journal of Medicine") described a case in which urticaria was coupled with shock and lowering of the blood pressure after exposure to the sun's rays, but not from artificial ultra-violet rays.

Here I should like to cite the following from an important article on solar dermatitis as it usually occurs in the white skin, by LAMB, SHELLMIRE, COOPER, MORGAN and KEATY in the Archives of Dermatology etc. (1950)

"The role which heat plays as a cause of solar dermatitis is not clear. Approximately 75 per cent. of the patients present *plaque-like lichenoid and scaly lesions*. Telangiectases are evident and induration is apparent. Pruritus may occasionally be the first symptom, and scratching may cause the induration. A reticulated pigmentary disturbance resembling poikiloderma of CIVATTE is frequently observed on the sides of the neck. No atrophy is apparent.

Two types of *contact eczematous solar dermatitis* are encountered: diffuse and localized. In the diffuse type, all exposed areas and in the localized type only certain exposed areas are involved, usually the cheeks; the backs of the hands may be free of eruption. *Prurigo aestivalis* or Hutchinson's summer prurigo, is characterized by recurrent eruptions of prurigo-like papules and nodules on the areas exposed to the light. The dermatological picture is varied and may change in the same patient. The first symptom is usually burning and itching of the skin followed by erythema and some degree of urticaria-like swelling. In prurigo aestivalis the areas of involvement are diffuse and if on the face the lesions usually involve the entire cheek and sides of the neck. In contradistinction, the lesions of *hydroa vacciniforme* follow a certain discrete line on points of the most intense solar exposure: the top of the ears, the malar region and the area over the bridge of the nose. The lesions of prurigo aestivalis on the arms are lichenified and diffusely pruriginous as opposed to the more or less discrete lesions of a typical case of hydroa ... ciniforme, with or without excoriation and lichenification. However, there is no cardinal sign in differentiation.

A rare group of light-sensitive persons complain of *erythema* without urticaria after the mildest exposure to sunlight. In addition to this group of patients showing transient eruptions, patients show *erythema multiforme-like lesions* or *erythema solare perstans*. The lesions are persistent and not transient, as in true *urticaria solare*. Differentiation from the ... vanescent, multiform type of l... pus erythematosus is difficult, but there is a definite seasonal remission which is not observed in the multif... rm type ...f lupus erythematosus. The white and red blood cell counts, the albumin-gl... obulin ratio and the sedimentation rate are in normal range in the multiform t... pe ... f s... lar dermatitis, whereas many of the evanescent types of lupus erythem... t... sus usually show leucopenia, secondary anaemia and reversal of the albumin gl... bulin ratio.

Phot... sensit... ity on ... n allergic basis from foods and weeds may be ruled out in most cases of solar dermatitis. The ... bsence of porphyrins in the urine of all patients t... st... d for them, eliminates these substances as photosensitizing agents in solar dermatitis. The creatinuria and moderately depressed 17 ketosteroids excretion may be ameliorated by the administration of testosterone-propionate or by stimulation of ... ndogenous androgen production in men by the administration of equine gonadotropics with resultant clinical remission observed for most patients. This observation shows, the decided effect of hormones on the pigment of the skin and on sen... ... ration to light (AND... EWS).

Histological ... minations ... howed non-specific inflammatory changes, oedema

in both the epidermis and the dermis and a cellular infiltrate about dilated blood-vessels in the corium. These changes were less pronounced after hormone therapy

In two severe cases of the plaquelike eruption the infiltrate was suggestive of mycosis fungoides. In five cases clinical evidence pointed toward the fact that fluorescent light is capable of both provoking and prolonging the eruption."

Dermatosis festonalis frontalis At the International "Health Problems" Conference of 1924 CASTELLANI called attention to a slightly itching erythema on some white patients foreheads, caused by chronic sunburn, to which he gave the name of *dermatosis festonalis frontalis*



101 "Lupus erythematosus" with atrophy in a mulatto Four years later the man revealed leprosy

(*Aars–Carayon*)

Ephelides and small pigmentary naevi occur very frequently among both whites and Indo-Europeans. In some cases no sharp dividing line can be drawn unless on the basis that naevi also contain naevus cells.

Lupus vulgaris in common with other forms of dermal tuberculosis, occurs rarely Usually "lupus of the tropics" is in fact cutaneous leishmaniasis Still all forms of cutaneous tuberculosis may occur in tropical countries, for which reason a separate chapter is devoted

to the subject in this book. Lupus erythematosus is occasionally found among whites in the tropics. IRGANG, in the Archives of Dermatology (1948) described the occurrence of *tuberculosis miliaris disseminata chronica* among Negroes. Tuberculids are extremely rare. There is a necrotic form of MANSON's pyosis which may resemble papulo-necrotic tuberculid.



102 Lupus in its morphological but not its aetiological concept because this case is due to tertiary yaws. Note ectropion.
(Wolff–Paramaribo)

Mycosis fungoides is extremely rare both in the tropics and in Europe. In Surinam, the author saw a native woman with an extremely widespread mycosis fungoides in the so-called tomato-tumour stage. The patient had no general morbid symptoms (Fig. 104). (See also granuloma gangraenescens and Fig. 76—80). Here I should like to draw attention to a most interesting feature which might be seen in any fatal skin disease. It is the "*vestimentum mortis*" or *cloak*

of death" is the unexpected "improvement in the patient's general and cutaneous condition a few days before death.

Diseases of the nails are found regularly but probably less so than in Europe. This certainly applies to onychogryphosis, which is probably a concomitant of varicose veins which in the tropics—and definitely among the autochthonous population—are found far less frequently than among the whites. The belief that the lunula of the



103 Scrofuloderma in the Negro
(*Peers–Nairobi*)

nail is always absent in the Negro is false. It is only much less evident than among whites. (For onychomycosis see Vol II).

Nodosités juxta-articulaires first described by LUTZ in Honolulu (1892) may occur among adults. They are usually localized symmetrically near the large joints but may also be found along the ribs and on the forehead. The aetiology is unknown, although VAN DYKE and OUDENDAL (in biopsy) found spirochaetes. Yaws and syphilis are most often

cited as causes, but these lesions are also found in seronegative individuals, particularly in rheumatism. Neither are they exclusively



104 Mycosis fungoides in a mulatto woman.

tropical since they have also been found in European whites. Pathological examination reveals fibrous tissue, and sometimes, but not in all cases, a homogeneous eosinophile mass in the centre of the



105 Juxta-articular nodosities. (Orr G Costa-Bela Horizonte)



106. Juxta-articular nodosities at the elbows of a Dutch farmer having suffered from rheumatism (quite common feature).

lesion. In some cases there is cystic or fatty degeneration, for which reason MENDELSON coined the term *xanthoma tropicum*. They should be distinguished from bursitis, exostoses, lipomata, lepromata, gummata, tophi and volvulosis. The treatment should be either extirpation or by antisyphilitics, the latter however being of doubtful value here.

Noma is quite frequent in the tropics, especially among young girls. In the majority of cases one finds it to be a primary non-febrile



107 Juxta- and non-juxta-articular nodosities. Note depigmentation of the sole of the foot

(Van der Zyl–The Hague)

gangrenous gingivitis. The flora consists of streptococci, staphylococci, sarcinae, corynebacteria, veillonella, ristella and (according to BOULNOIS and RABEDAORO), invariably also spirochaetae Vincenti. Thanks to vitamin-C and antibiotic treatment, the mortality is now comparatively low. (BOULNOIS and RABEDAORO in Semaine des Hôpitaux de Paris, 1950) (See also *trench mouth*)

Orf, sheep pox or *sheep thrush*, a contagious viral pustular condition

of sheep may rarely be seen in man. Notwithstanding the fact that I have only seen a single case in a Dutch woman farmer having fed a motherless lamb which suffered from sheep pox, I think it is useful to draw the attention to it, since sheep pox also occur in the tropics. The disease shows one or more solid, painless framboesiform or naked vegetative lesions, covered with some white exudate and it is localized on the fingers or any other part of the skin, which



108. Noma in boy suffering from kala azar
(*Kat-rnelkebogen—Jerusalem*)

has become infected. The disease which may easily be confused with any other vegetative condition heals spontaneously.

Parotitis epidemica usually unilateral which may affect the parotids and the testes is not rare in the tropics. The orchitis should be distinguished from malarial orchitis (purulent) and bilharzia orchitis (fistulous). A chronic bilateral enlargement of the parotids of unknown aetiology has been reported by FONTOYNONT among natives in Madagascar calling it *mangy*. It has also been described in Egypt, the

Belgian Congo and in the State of Rio de Janeiro, where it is common among descendents of African slaves. (NERY GUIMARÃES in O Hospital 1948) In such cases one should think of melioidosis (*q v*)

A great number of the patients also suffered from pellagra. (I did not see such a condition among a great number of pellagrins, but a life long deficiency may perhaps cause it)

Pemphigus vulgaris is sometimes reported in the tropics (Fig 110) even in its combination with lupus erythematosus when called SENEAR USHER syndrome (Fig 111 and 112). The *epidemic* Brazilian foliaceous pemphigus called *fogo selvagem* (*i.e.* wildfire) is probably not a "true" pemphigus (acute pellagra with infectious eczematoid dermatitis: SUTTON and SUTTON). LINDENBERG (Yearb 1938) regards the condition a viral disease GUIMARAES and MOURAO described gonadal disturbances in their male patients. (Bras. med. 1942) *Pemphigus tropicus* is a pyoderma (*cf* MANSON's pyosis). One sometimes comes across a



109 Framboesiform lesions of orf or sheep pox.

form of bullous dermatitis caused by the sap of the manchineel tree (Hippomane manchinella) in the West Indies or the renghas in Indonesia, which we have already mentioned (*cf* dermatites forestières).

Pigmentation—apart from that found in naevi—is of frequent occurrence, if for no other reason than that pyoderma among the dark races tends to be followed by hyperpigmentation. Melanosis caused by pellagra was often found in internees and prisoners of war. Another interesting phenomenon is *chloasma*, which is fairly frequent among both white and coloured people. It may be due to photo-sensitization of the skin caused by the use of eau de cologne against the heat but there is also a form of chloasma, the cause of which is

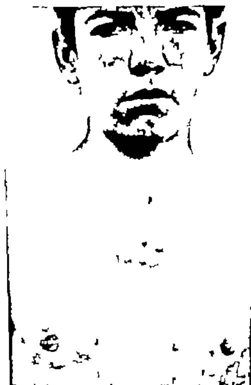


110 Pemphigus vulgaris in a Tamil woman. *(Fasal–San Francisco)*

hard to explain, and which, without there being a demonstrable vitamin-C deficiency, responds very favourably to vitamin-C treatment (high doses). SZENT GYÖRGI, SCHROEDER and EINHAUSER are of the opinion that vitamin C reduces the dopa reaction and the formation of melanin. According to JADASSOHN and SCHAAF, vitamin C furthers the formation of melanin in the adrenal gland, but this reaction—according to these authors—can be countered again by vitamin D. (See also porphyria, page 113.)

Berloque or *berloque dermatitis* around the mouth or on the hands may be caused by eating or peeling citrus fruit, or by the use of

hair lotions (Fig 128) *Melanosis Riehl* comprises more or less the following pigmentations (a) *melanodermitis toxica* which I consider to be identical with breloque dermatitis and which is caused by medicamentous discolorations sometimes via photo-sensitization (b) *poikiloderma reticulare* (CIVATTE's disease) a reticular pigmentation with telangiectasiae on the neck and (c) *melanosis* RIEHL in the re-



111 Senear Usher syndrome in Brazil: Seborrhoic type.
(Osw G Costa—Belo Horizonte)

stricted sense of the term, with which are classed different discolorations which do not come under either (a) or (b), and which cannot be diagnosed as either *chloasma* or *Addison's disease* In chloasma it is especially essential to examine the nipples, linea alba and genitals In Addison's disease the mucous membranes require particular

inspection. In all odd pigmentations one should think of pellagra.

Mongolian spot (Malay *tanda*) is a common pigmentary phenomenon found in the tropics in very young children of Mongolian, but also of Chinese, Indonesian, Negro and European descent (EPSTEIN Prague, ½ per thousand). It may look as if the child had a bruise left over from a fall or a thrashing because the pigmentation, being situated deeply in the skin, shines through with a bluish tint. The spots are mostly found on the buttocks and the lower part of the back by the end of the fifth year of life they are already less distinct, after which they gradually disappear completely (See also "blue bottom" page 28)



112 Pemphigus vulgaris (verrucous type).
(Orr G Co te-Beh Horkeate)

Ret n g Pi s (The East African Med. Journal, 1946) the following is of mp rt nc I he ncidence of the *blue spot* among Jewish children in Palestine varied f m 30 4 pe cent in Jemen tes to 2.4 per cent in Mediterranean Jews and 0 47 pe ce t in hildren of Eastern European descent. (HELEN K. GAN). The in cidence m g Af ican children appears to vary in different parts of the world The spot ma be f und outside the area of predilection, *e.g.* on the thorax. Pie found he blue pe n nearly 90 per cent. of the East African boys and in 75 per cent of girls But the n ce has also been found Among I dian children Piles found the f ll wing figure H ndoos 92 per cent., Mohammedans 75 per cent Sikhs 88 per cent nd Goans 96 per cent. The blue spot is not found in adults but a related condition the blue nae us of JAD SSO or TIECHE may ccasionally be seen. *It develops aft birth and has no te of predilection.* Histologically the blue spot is characterised by the presence of melanoblasts in the cutis. It is thought that

they represent vestiges of a phylogenetically ancient pigmentary layer. This mesodermal pigmentary layer persists in many animals, e.g. in the East African Cercopithecus and Rhesus monkeys.

In Negroes one sometimes finds in addition to the Mongolian spot, a dark discoloration of the gums. This melanin line may easily be confused with a *bismuth fringe*. In about 25 % of Sunda Negroes the



113. Widespread melanosis of unknown origin in a Javanese cured by high dosages vitamin C.

pigmentation passes also to the tongue (CHALMERS and MACDONALD). BREYER, LIGNAC and VAN DER VEER published a study on the subject in the Acta Leidensia (1940).

We may here mention the chloasma caused by the atomic bomb (at a distance of 1 ¼ miles), and called *Hiroshima mask*. Leukoderma (both with and without atrophy) is also known to have been due to the influence of the atomic bomb; as in the case of vitiligo, it is surrounded by a hyperpigmented zone. This is due to one of the many

side-effects of the atomic bomb: an extremely intensive artificial sunburn which, at a sufficient distance, becomes "artificial sunlight pigmentation".

Pityriasis rosea is fairly infrequent in the tropics: less frequent, at any rate, than in Europe. An interesting case is the following. On one occasion, when many P.O.W.'s found themselves without any clothes at all—especially after the sinking of a large number of troopships—the Japanese military authorities, in a fit of benevolence, supplied the



114. The back of the same patient. There was no hyperkeratosis. The photograph was made after two soft soap bathes.

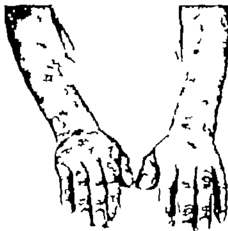
men with a garment consisting of a loin-cloth measuring about 30" by 12" cut from curtain material in all sorts of colours. After having worn an orange-coloured piece of cloth for about a fortnight, one of the P.O.W.'s appeared with a distinct initial lesion just below the umbilicus, followed shortly afterwards by the exanthema. LENNHOFF in the Acta Dermato Venereologica (1948), reported the discovery of spirochaetae in eighty cases of pityriasis rosea.

Porphyria with bullous lesions corresponding to the types epidermolysis bullosa and hydroa aestivale are quite common in the Bantu

population of South Africa. MARSHALL, Johannesburg (personal communication) has seen many cases presenting simple or dystrophic lesions which he prefers to describe as *"porphyric bullous dermatosis"* In some cases bulla formation is not seen, but the skin is fragile and easily scraped off or is abnormally liable to minor infective lesions In such *formes frustes* the scars remaining after healing resemble those left after bullae and their appearance and distribution are of diag



115. Chronic porphyria in a Bantu woman showing "chloasma" and hypertrichosis. *(Kern—Johannesburg)*



116. Chronic porphyria in Bantu woman. Blisters scars and area of pigmentation. Nail changes and hyperkeratosis over the knuckles can also be seen. *(Bersen—Johannesburg)*

nostic significance. In a number of cases of chronic porphyria, a warty hyperkeratosis of the skin over the last two knuckles of the fingers may be seen. Hyperpigmentation of the exposed skin, some times resembling that of pellagra, is common. Hypertrichosis of the face is often seen in women, and was present in a few male cases. Chronic porphyria also exists in the European population of South Africa and the incidence appears to be higher than in Europe (with the possible exception of Sweden) Acute porphyria is rare in the Bantu population, but relatively common in Europeans Often there is no clear-cut line of demarcation between the chronic (cutaneous)



117 Psoriasiform yaws.
(Aars–Curaçao)



118. Chromomycosis due to Hormodendron pedrosoi.
(Barg–Mexico City)



119 Madura foot.
(Dostrovsky and Sagher–Jerusalem)



120 Melanocarcinoma
(Prigs Jogjakarta)



121 "Epidermophytosis" a clinical concept often not covered by the mycological finding



122. Shoe-lining eczema so often taken for epidermophytosis, particularly when secondarily infected with fungi.



123 Secondary syphilis
(Zoon–Utrecht)



124 Unilateral keratoma sulcatum plantarum pedis.
(Fasal–San Francisco)

and the acute (abdominal and nervous) types. A case of congenital porphyria has been discovered by FINDLAY and BARNES (Lancet, 1950). This form may show bullous lesions of exposed parts, hyper pigmentation, hypertrichosis and brown staining of the permanent teeth, as well as pigmented bones (fingers!), progressive anaemia and splenomegaly. Deformities of the hands may be mistaken for leprosy.

Prurigo nodularis is relatively frequent: in the P.O.W. camps we saw large papules mainly on the uncovered parts of the body and probably



125. Psoriasiform quininoderma (perhaps acute psoriasis) within one week time following tentamen aborti with 30 tablets of quinine in a 40-year old woman, who has not suffered from psoriasis previously. The face was also affected.

due to the bites of bed bugs. KAYSER thinks it quite possible that cases have been described under the diagnosis *cras cras* or *kra kra* which in reality should have been classed as prurigo. He found this affection in one per cent. of native sufferers from skin diseases, particularly among children between six and fifteen years of age.

Pruritus is as frequent in the tropics as in Europe; broadly speaking at any rate one finds no significant differences. The excessive use of

soap ("prickly heat soap"!) is sometimes an important cause (*vide* zoonoses) Pruritus *ani* is strikingly less frequent both in Indonesia and the West Indies KAYSER attributes this to the natives and European settlers habit of chebokking" *i.e.* washing the anus, instead of using paper This may apply to Indonesia, but "chebokking is not a general custom in the West Indies I personally attribute the absence of pruritus ani to frequent bathing by which the anus is daily cleansed.

The word *gatel* for "itch" is, next to *sakit kulit* for "sick skin" about the most elementary word in Indonesian dermatology Just as *kras krassi* next to *siki skin* is in Surinam, and *kuskiments* next to *calor* or *braed* in the Antilles

Psoriasis is found among the native population in Europeans, less frequently than in Europe but one does meet with it occasionally I found a Java Netherlands ratio of $\pm$ 1 30 In Jakarta the number of psoriasis patients was 1¼ per thousand skin disease patients (VERBUNT) Among the Dutch, psoriasis appears to be less frequent [1] in the tropics than in the Netherlands but the affection is none the less found fairly regularly *and sometimes even in a more severe form* than had previously occurred in the Netherlands *Removal to the tropics offers hope but definitely no guarantee of improvement* In the "hunger camps" psoriasis usually abated, only to revert to its old form after the war [2] Psoriasiform psanids may be found in yaws [3] We are also reminded in this connection of psoriasiform syphilis.

A case of acute "psoriasis" which manifested itself in the sites of predilection, but also on the face, was observed by the writer in a British officer, following a strong quinine treatment of malaria, and another case in a white woman who had taken 30 quinine tablets in one day (dose unknown) in a tentamen aborti. (See Fig 125) (See also erythroderma and "witkop")

Psychodermatoses I should do less than justice to the claims of completeness if, in a book appearing in the present decade, I abstained from saying a few words on this subject. After all the experiences we have

[1] Maybe on account of the medical examination before departing to the Indies?
[2] SIMONS, R. D G PH., *Journal of Inv stig Dermat.*, 1949
[3] V BRUSTO DEM *Acta Tropica* 1947

had with "Konstitutions Pathologie" dietetics calcium deficiency focal infection and the like, a certain reserve in this respect does not seem out of place. None the less, we know that flushing sweating goose-flesh, self mutilation etc., are intimately bound up with the psyche, and that even the virus disease verrucae vulgares may be cured by suggestion. SIEMENS' phenomenon of *sanatio spontanea nosocomialis* from hospitalization alone, may be due either to allergic



126 Multiple injection wounds in Chinese morphinist, forming an odd dermatosis.
(Elsbach-Bandung)

reconditioning of the patient or to a psychogenic affect. It may also be due to the fact that the patient has been removed from an unknown source of infection (strophulus?) But attributing a naevus ("birthmark") to the mother having been startled during her pregnancy by a dog etc. or to her desire for some special food (for which reason birthmarks are called "lostou" meaning "desire" or "appetite" in Guiana) may be consigned to the realm of fables as well as has been done with leprous macules which were attri

buted to dreams. The view that the patient constitutes a psychosomatic integer should not be allowed to preclude the most important invader of this entirety *i.e.* any micro-organism or antigen. I am fully aware of the many striking cases of skin disease due to psychosomatic influences as I have been of those from hidden focal infections but I am not definitely convinced that the seborrhoic patient is no easy talker" that "the acne patient prefers classical music to jazz" and that 60 per cent. of only psoriasis patients are emotional (and who would not be emotional if he had psoriasis!)

WISE and ENGLISH (Ref GAY PRIETO in Der Hautarzt 1951) even



127 "Giftspots" This most popular sign of calcium deficiency intoxication, mendacity etc. disappointed medicine men, when it proved to be no more than a sequel of bad manicure

speak of an organic cutaneous language, in which pruritus represents anxiety urticaria anxiety plus anger, pruritus ani homosexual tendencies (what about oxyuriasis, haemorrhoids and the fact that pruritus ani is much less common in the tropics than it is in Europe?)[1] Many diagnoses in this respect should be regarded a sequels of "*das entsti-*

[1] TWISTON DAVIES stated in the Brit. Journal of Physical Medicine 1951 that he never got no for an answer if he asked a young man with chronic lichenification of the perineum, if he is the only son of a widow

sche und undisziplinierte Denken in der Medizin' (undisciplined and wish ful thinking)

Sudden greying of the hair in the space of a single night has often been related, but never substantiated. (The hackneyed story of Marie Antoinette, who turned grey during the night before she went to the guillotine, is based on the fact that she had to take her wig off) During the last war I did not find a single case of sudden greying among thousands of troops who had been frightened by bombing, shipwreck fighting and especially the Kempei torture. Early greying



128. This strangling psychodermatosis having been under psychiatric treatment proved to be a breloque-dermatitis from hair lotion. The patient, living in I a, was told that the pattern obviously showed an attempt of strangling by her rival who applied gouna gouna (black magic)

which, however took some years was seen in rare cases and was probably due to vitamin deficiency

Despite bad psychological conditions we found that psoriasis and many cases of eczema healed spontaneously in the majority of cases, which is contrary to or certainly not supporting the opinion that these dermatoses are due to a psychological trauma or complex. On the other hand it is important to state the sudden cessation of menstruation in the female internees and the sudden re-occurence after the

end of the war The psychosomatic factor—when present!—is most probably not a mere psychic *affect* but a *conflict*

In determining the diagnosis of a psychodermatosis the following factors should be kept in mind

a the psychic factor must be diagnosed, as is done with every other aetiological factor If the psychic factor is not shown to be an aetiological factor then the diagnosis however plausible, still remains indefinite.

b when a psychic factor has been demonstrated it is still necessary to consider the possibility of *coincidence* A person after all, may have psoriasis, carcinoma or syphilis quite independently of his neurotic or psychotic conflict, just as a carcinoma patient may show a positive Wassermann reaction. In other words, the diagnosis of a neurosis or psychosis is of no irrefutable topical value in the case of a skin disease.

c a sharp distinction must be made between the psychic factor as a causal *(psychodermatosis)* and provoking *(dermatoneurosis)* agent, and the question whether the patient develops a skin disease due to his nervousness or is nervous because of his disease. Especially in cases of shirking military service or work, it appears that the patient may be able to maintain his disease or may become "der mato—prone"

By and large one should guard against labelling a disease psychosomatic merely as an "embarrassment diagnosis" Evidence of the cause of one case does not necessarily lie in the cause of another case [1]

Purpura is seen in the tropics as well as in Europe. BONNE saw purpura and epistaxis in malaria, without any treatment having been given. (Med. Maandblad, 1947) There are three special forms that should be mentioned they are (a) *kurab* (already referred to) (b) the *pellagra haemorrhagica* described further on in the book, including a case of purpura solaris provocata, and (c) *tropical thrombocytopenia* or *onyalai* also known in Africa by the names of *akembe kafindo* and *chilopa* This

[1] See also R. D G PIL SIMONS Dermatitis artificialis en goena goena — (Geneesk. Tijdschr v Nederl Indie 1939) in which a breloque dermatitis from eau de cologne was regarded as the print of clutching hand from black magic. See also an interesting psychosomatic study on eczema by WITTKOWER and EDGELL in the Arch of Derm. & Syph., 1951

disease starts fairly acutely with purpura of the skin and mucous membranes and death sometimes follows as early as a week afterwards. The tongue and the parotids may be swollen, and practically all organs at post mortem seem to have extravasations There is anaemia with thrombocytopenia with a prolonged bleeding time, without the clotting time being markedly retarded. The aetiology is unknown. DUTTON (J.A.M.A. 1938) ascribes it to allergy to citrus fruit but in Indonesia and Surinam, where citrus is eaten and handled quite regularly the disease is not known. GELFAND (Trop Dis. Bull. May 1950) in an abstract from an article by JELIFFE on this disease, suggests that onyalai may be a clinical syndrome and not a distinct disease, and that the onyalai blisters may occur as specific lesions in various haemorrhagic conditions in Africans

Treatment consists in injecting 20 ml of the patient's own blood intramuscularly or in blood transfusion. Splenectomy does not always appear to be of much use

It is important to know that purpura in a dark skin is often followed by haemosiderin pigmentation.

Pyoderma is dealt with in some detail in the chapters II V VI XIV XV and XXV

Pyosis Mansoni occurs epidemically in hot climates, especially among white children. In the cold mountain regions in Java this pyoderma is far less frequent, as is also the case with prickly heat while in the West Indies too pyosis is relatively rare. A special form is that described by CHRISTOPHER in his *Textbook of Surgery* and which is caused by haemolytic streptococci. We saw two cases of this in Sumatra (Pakan Baru) The skin of the lower leg and over the knee and tibia showed blue discoloration and was more or less tra[illegible] ent owing to the serous exudate underneath. There was widesp[illegible] t dermolysis the epidermis could be painlessly torn open over [illegible] e lower leg when the almost clear fluid came away The patient a euphoric state and died in this condition within three days. no toxic cl uding of consciousness until the v[illegible] t momen the lymph glands in the groins are already swo[illegible] is gene late to save the patient's life by amputation

Recklinghausen's disease is not often seen its [illegible]) is ab[illegible] same as in Europe. See also elephantiasis

Rhinoscleroma sometimes called *scleroma respiratorium* also occurs in the tropics. It was first described in South-East Europe, and occurs there still. The klebsiella rhinoscleromatis is probably identical with the klebsiella granulomatis formerly called DONOVAN s capsule coccus



129 Recklinghausen s disease in a Chinese in Java.

of venereal granuloma. Both diseases will be fully dealt with in this volume. (See also page 9).

Of scarlatina it may be said that it occurs neither in Indonesia nor in the Antilles or Surinam, despite the ample presence of streptococci (KEIZER) The cases observed before the war were probably scarlatini form toxicoderma (see also chapter 2).

Scarlatiniform exanthemata (not to be confused with prickly heat) may be found after the use of among other things quinine The more

modern atabrine sometimes produces erythematous spots (*cf.* also under drug eruptions).

Schistosome or cercarial dermatitis is caused by the cercariae stagnicolae (definite host: the canary) penetrating into the skin of birds or mammals. Schistosomes are an itching erythemato-papular or urticarial reaction developing about 12 hours after the penetration. It may last for about a week, providing no secondary pyoderma occurs. Adenitis may be present. The disease has also been reported in Europe (lake of Constance). There is a fairly exhaustive and detailed article on the subject by CORT in the American Journal of Hygiene (1950).



130. The "tropical seborrhoic state" shows a dry squamous condition of the alae nasi, and the cheeks and at the both sides of the raphe scrotti. When in an incipient form it might not be recognized as a feature of deficiency of the vitamin-B complex. It should of course be distinguished from lupus erythematosus.
(Gopalan-Connor)

Scleroderma doubtless also occurs in the tropics. I saw one case in Sumatra, on the back of a light-coloured male, and surrounded by a distinct lilac ring. The man had also alopecia areata (not sclerodermatic), which, after being cured reappeared in another place on the head.

Seborrhoea is fairly frequent, but definitely less so than among whites (*cf.* also seborrhoic state, which is probably due to deficiency of the vitamin B_2 complex).

Senear Usher syndrome: vide pemphigus.

Sodoku or rat-bite disease, is mentioned here only for the sake of completeness. It begins with a (sometimes gangrenous) primary



131 Strophulus affecting a Javanese adult after arrival in Europe. *(Siemens-Leyden)*

lesion (*i.e.* the rat-bite) followed 3 weeks later by relapsing fever and—usually running parallel with this—exanthema, characterized by erythema with disseminated papules. It is caused by spirochaeta

morsus muris The therapy is the same as in yaws. (See chapter 10)

Strophulus is rarely met with in the tropics. An interesting point is that many Indonesians who came to Holland (including adults) contracted strophulus soon after arrival. Whether this was due to the change in diet is open to question since the immigrants had been taking Dutch food on board for at least a month previously A more plausible theory is that of BOTTER, *i.e.* that strophulus is an infectious disease to which the adult becomes immune and there being practically no strophulus in Indonesia, immunity against it must be equally rare.

Syphilis is found very frequently and in its various cutaneous forms, which may easily be confused with different other dermatoses, especially with yaws leishmaniasis and different types of ulcer In rare cases there may be an extragenital affection which, unless one is prepared to suspect its presence, may be taken for yaws or leishmaniasis On the darker skin, the early secondary syphilitic roseolae often escape detection as such, and the white man may attribute them to prickly heat, shrimp-poisoning, or calcium deficiency When the spots get older they appear as dark brown or black patches (haemosiderin pigment) Frequently there is simultaneous secondary syphilitic angina On the other hand, a more widespread papular or pustular acneform eruption or a corymbiform group of papules or pustules should definitely be regarded as indicating the presence of secondary syphilis especially when they are also found on the palms of the hands or on the soles One sometimes sees white or dark spots on the neck, of a "collier blanc (or noir) de Vénus" which might wrongly be taken for tinea versicolor because they are a luetic phenomenon. *Alopecia syphilitica* may easily be confused with alopecia caused by folliculitis, or conversely This subject will be fully dealt with in chapter 5

Tattoo *Vide* page 50

Toxicoderma *Vide* drug exanthemata.

Tuberculosis of the skin has been described in a separate chapter See also lupus vulgaris

Tularaemia is often described in books on tropical medicine but the disease has most frequently been reported in Scandinavia, America, Japan and Asia Minor It is a disease of rodents caused by Pasteurella tula

rence, which is transmitted to man by the bite of a chrysops, bed bug tick mosquito etc. The disease may also be transmitted by water or meat infected by the excreta of rodents It may be taken for plague or rat bite fever because of the adenitis and primary lesion. The diagnosis should be established by recognizing the specific pasteurella. The febrile roseolar exanthema of tularaemia, in association with the adeni



132. Lentigines in Javanese woman.

tis, lymphangitis and conjunctivitis is by no means of sufficiently diagnostical value.

Tumours (neoplasms). The only reason why tumours are found relatively infrequently among whites in the tropics is because these people usually retire on a pension and return to the mother country before reaching the "tumour-age" What is called *farmer's skin* or *tropical skin* which may show multiple small carcinomata, is practically never seen in dark-coloured races and relatively infrequently in whites, when the latter do little or no farm-work in the tropics Among the white fishing population of St. Martin (lesser Antilles) however, carcinoma of the face is far from rare one sometimes

sees a patient with three or more growths (HARTZ). In albinoes there is also a certain predisposition to skin carcinomata.[1] HAZEN and FREEMAN (Arch. of Derm. and Syph., 1950) state that basal cell cancers are very rare in the negro race, whereas squamous cel



133 "Tarzan" as he is called in the desa (native village) owes his "pitheton ornans" to his widespread verrucous pigmented naevi. On the lower arms some amelanotic (i.e. non-pigmented) papules.
(Pruys-Jogjakarta)

cancers are not infrequent. Melanoma is said to be rare, but in my opinion it is more often seen in pigmented races than among whites. *Melanotic carcinoma* is sometimes called melanotic sarcoma, because the histological picture is very vague. Other synonyms are melanoma,

[1] Although the *tropical skin* is not confined to the tropics, I should like to draw attention to a subtype, which is more frequently seen in blond women. It is the triangle of a sharply defined lichenification with wrinkles, dry hyperkeratosis and freckles, that is "saved" by low-necked dress.

lentigo maligna, naevocarcinoma and melanotic naevus or melanotic freckle (*cf* Volume II)

Melanoma may appear anywhere on the body but has a preference for the face, the toes ("tourniole mélanique") and soles—the last especially among coloured races In these cases one is readily inclined at first to take it for the dirt tattooing of an old wound. An interesting problem *is that of melanoma of the eyes*.

Apart from naevi and the common dark freckles, melanoma might also be confused with (a) pigmented basal cell cancer or black rodent



134 Kaposi's haemangiosarcoma, one out of 60 patients in Johannesburg. *(Kamlner and Murray–Johannesburg)*

ulcer (b) common basal or squamous-cell carcinoma in dark-skinned individuals (c) verruca senilis or verruca seborrhoeica (which, for that matter is seen far less often in dark-skinned individuals than in Europe) (d) naevus verrucosis, and (e) genuine coal-tattooing" which occurs fairly frequently among dark-skinned *stokers*. *When* ever melanoma is suspected the entire affected part should be radically excised far into the healthy tissue Biopsy acts, as is well known, as a stimulus to growth, for which reason melanoma is also called ***noli me***

tangere ("touch-me not"). In fact, a case of melanoma of the foot ("merely *tumeurs mélaniques*") at once suggests seriously the exigency of immediate amputation of the whole leg from the hip joint and even then this usually comes too late.

Other malignant tumours have also been described here and there as occurring in the tropics. *Sarcoma haemorrhagicum idiopathicum* KAPOSI occurs, according to HAZEN and FREEMAN, as frequently among negroes as among whites. It has been described by, amongst others,



135. Kaposi's idiopathic sarcoma haemorrhagicum of the thigh of a Chinese in Java.

KAMINER and MURRAY in the South African Journal of Clinical Science (1950). These authors found frequent cases of this disease among men, and they suggest the possibility of a genetic factor. PAUTRIER and LASSUEUR first reported affection of the internal organs, particularly of the gastro-intestinal tract (Dermatologica 1946). It is of great importance and interest that this tumour can most probably disappear by penicillin therapy (4 000 000 μ).[1] An important point

[1] An excellent article on this subject has been published by MCCARTHY and PACK in Surg. Gynec. and Obstetr. 91/4 of 1950.

is the rare occurrence of carcinoma penis at any rate there, where circumcision is customary *Bowen's disease* and *pagetoid*" (a superficial type of basal cell carcinoma, without metastases of the lymphatics) are not often reported. Paget's disease, *i.e.* genuine carcinoma mammae, either with or without dermal metastases, is on the other hand, far from rare. Two more "exotic" carcinomata deserve mention, *viz.* "*kangri basket cancer*" a non-metastasizing squamous-cell carcinoma of the abdominal skin occurring in Kashmir and Tibet, where people



136 Oral carcinoma from chewing betel nut ("sirih").
(Prijs–Jogjakarta)

are wont to keep their belly warm by means of a basketful of red-hot coals and the squamous cell *sirih-chewer's* or *betel-nut carcinoma* on the inside of the cheek. The reasons for this sirih-chewing are, that it stains the lips red that the nut and the leaves of the betel-pinang or areca catechu palm are supposed to have a refreshing effect and are said to give the face a slight "nitmold" complexion.

In conclusion, a remark concerning carcinoma in old ulcers this should not be confused with the (also histological) picture of a pseudo-malignant growth, even when coupled with horny pearls, as sometimes found in chronic ulcers. Cutaneous yaws too may imitate carcinoma. (Further details are given in chapter 7)

Lentigines are benign soft papules mostly occurring on the face They are frequently seen on whites, Indo-Europeans and natives of middle age and older

Ulcers Among the many different ulcers found in the tropics, those of malignant and tertiary syphilis take an important place. WASSERMANN's reaction will usually be positive but so it is in yaws The diagnosis is difficult. If possible, it is advisable to make a suboccipital or lumbar puncture. A physician with experience in this operation can do it as rapidly as a blood test a long not too thick needle (either with



137 Melanoma papule behind earlobe of Negro woman.
(Fasal San Francisco)

or without a mandrin) will then suffice. In ulcerating syphilis, which usually dates from three or more years back examination of the CSF is indeed, essential It should be borne in mind that some one with a non-syphilitic ulcer may still have syphilis A positive Wassermann reaction therefore is not a 100 % guarantee of the ulcer Response to some injections of an arsenical is of more significance in this respect "*Syphilis africaine et asiatique*" as well as syphilis in tropical America, sometimes differs from that found in Europe, a fact which is evident from the pigmentary changes in dark skinned races Organic syphilis including neurosyphilis does doubt

less occur in the tropics, in contradiction to what used to be assumed.

A separate chapter deals with tropical ulcers etc. It is of some importance to state at this point that phagedaenismus does not appear to be the exclusive monopoly of the fusospirillary symbiosis in PLAUT's (VINCENT's) symbiosis in fact, it appears that pyococci in some cases cause similar ulcers. Cutaneous amoebiasis too may have a phagedaenic character

Urticaria occurs in the tropics as in Europe. In the tropics it is often —rightly or wrongly—blamed on the mango and other fruits and, to



138. Non-itching and non-evanescent urticaria may be an acute lepra reaction as in this Hindustani boy with previous tuberculoid leprosy

judge by the "papiemento" term "*pichi bichi*" even on "urine worms" Urticaria may be caused by different insects, especially in persons newly arrived in the tropics and evidently not yet immunized. This is particularly obvious in cases caused by the bite of the mosquito (Aedes aegypti) and the sting of Trombicula batatas which will be discussed further on. DOSTROVSKY has described an endemic urticaria named *harara* resulting from the bite of Phlebotomus papatasii Cases of *urticaria y paludismo* are known which were not caused by either atabrine or chinine, but, on the contrary cured by these drugs this is the

reason why PUMAR omits y from the name and suggests the possibility of its being malarial urticaria. Non-evanescent, fixed urticaria or Quincke's oedema is often met with in the tropics and in East and West frequently attributed to the bite of a cockroach. Also "three-day sandfly fever" or papataci fever" due to a virus from the bite of the phlebotomus may reveal Quincke's oedema of the lips, genitals or around the joints. In some cases no oedema or urticaria



139 It is said that the "Sepou" of the caribbean Indians present varicose veins, but these "garters" are mere ornaments.
(Stadel-Surinam Trop. Inst. Amsterdam)

occur but only a severe evanescent and wandering pruritus may be present. There is no adenitis. In the more pronounced cases there is pressure on the eyes and the patient suffers from an influenza like condition with or without stomatitis.

Because pilgrims visiting Mecca often pay their toll with the incipient form of the disease, it has been called Salaâm (salute) Mecca". The writer saw a case of QUINCKE's oedema of the penis and one on the vulva, caused by hetrazane treatment for filariasis Bancrofti (I *vide* also dermatites forestières.) In cases of non-evanescent urticaria one should always think of tuberculoid leprosy in reaction.

Varicose veins, varicose eczema and varicose ulcers are less frequent among the native population than among Europeans, which might perhaps be attributed to the fact that the natives walk much more, and/or barefooted, than Europeans. Some American Indians wear a tight band both above and below the calf, a custom they start while

still young The band is intended as an ornament, and not, as is sometimes thought, as a preventive against varicose veins Varicose veins are regularly found in Europeans living in the tropics a fact which is an "eyesore" especially to the women, who often walk without stockings.

There is much similarity between varicose eczema and *hypostatic dermatitis* coupled with oedema and purpura as a result of thrombo phlebitis. In this case, although the patient may have varicose veins as well, which admittedly have a bad influence on the process they certainly are not part of the syndrome as such. Chronic hypostatic dermatitis may result in elephantiasis, which is sometimes confused with the bubu or Barbados leg of filariasis Bancrofti.

One remark is apposite at this point, *viz* concerning SCHAMBERG s disease, *i.e.* a progressive purpuric pigmentary dermatosis, usually occurring on the legs without any connection with varicose veins. The name should not be confused with SCHAMBERG s disease for cotton seed dermatitis due to Pediculoides ventricosus (*cf* Zoonoses).

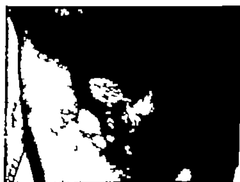
Variola is still of regular occurrence in the tropics (*vide* chapter 30) and the same applies to *varicella* Fig 95 shows the case of a girl whose little sister had varicella, and who had an eruption after sun-bathing, far less widespread on the parts protected by the swim suit than on the exposed parts. A *varioliform* or *varicelloid* eruption may be provoked by *Pfeifferella whitmori* a gram-negative bacillus which causes necrosis in practically all organs (except, perhaps the brain) resulting also in different internal disorders and their accompanying complaints.

Varioliform vesicles may occur in *melioidosis* which is the cause of about 200 deaths a year in the Malay Peninsula (Brit. Med. Journal, 1947) but, it appears it may sometimes be cured by sulphonamides. The infection, is perhaps caused by food vitiated by Bacterium whitmori introduced by rats. Apart from general phenomena such as diarrhoea fever and alopecia the disease is characterized by a kind of parotitis and varioliform vesicles with abscesses of the skin as well as in the liver and spleen.

Verrucae in all forms and *molluscum contagiosum* are found quite regularly in the tropics[1] (see also however under histoplasmosis) In Aruba I

once saw a case of molluscum giganteum, which suggested the possible presence of verruga peruviana. The colour however was not red, and the papule was umbilicated. (See also *Nuñez Andrade* disease)

Vitiligo too is seen regularly and even more distinctly among the dark races than among whites—which is only natural. It should not be confused with achromia as found in tinea and pinta, or more especially with the white spots in tuberculoid leprosy. I think that many cases of achromia in the tropics which are diagnosed vitiligo and particularly tinea albigena are in fact pinta and the vice versa. The condition called tinea albigena has proved to be pinta or vitiligo



140 Vitiligo and leucotrichia on the neck of a Chinese boy on Java

secondarily infected with Epidermophyton floccosum, the pleomorphic form of which the author NIEUWENHUIS had not recognized as such. (SIMONS) The miliaria in prickly heat sometimes become pustules, in which case they leave small, white cicatricial spots on the dark skin, which give one the impression of *white spot disease*. Something similar moreover may be seen as a result of varicella, *i.e.* numerous atrophic spots the size of a pinhead (see Fig. 26 page 43). Vitiligo (or albinism) of the glans penis was described by KAYSER, in his work containing reprints of lectures on tropical skin diseases, and by SIMONS in the book on venereology and genito pathology. It is not impossible that these white spots originate from primary lesions, although they do not reveal atrophy.

[1] BARRACK suggested mollusca contagiosa being sometimes perhaps transmitted by bird mites. (Austral. Journ. of Derm., 1951)

Witkop or *dikwakwadi* a psoriasiform condition was firstly described in 1910 by MACARTHUR and THORNTON at the South African Medical Congress. They considered it to be a manifestation of congenital syphilis.

Although MITCHELL (South Afr Med. Rec., 1915) found Acho-



141 Witkop or dikwakwadi in a South African Negro. A psoriasiform condition in congenital syphilis.
(Marshall–Johannesburg)



142. In these cases of Witkop RODHAIN found Achorion schonleini.
(Rodhain–Antwerp)

rion schoenleini in some cases as did also RODHAIN (see this book, vol II) FRASER (Brit. Journ. Derm., 1922) and MARSHALL & WILSON (South Afr Med. Journ., 1949) again considered the possibility of witkop being a manifestation of congenital syphilis.

They found positive blood tests in all their cases no scutula, no mousy smell and no fungi The condition healed under antisyphilitic treatment but also spontaneously (as also does favus) leaving either a normal scalp or atrophic scarring (called *kaalkop* i.e. bald head) which is common in favus.

Xanthelasmata occur in the tropics. Treatment by diathermy must be advised against, on account of the risk of keloid formation which, it appears is greater in coloured than in white individuals In Singa-



143 Carcinoma in xeroderma pigmentosum.
(*Sagher Jerusalem*)

pore we saw a woman with a spectacle shaped keloid round the eyes which was supposed to have been caused by the diathermic treatment of xanthelasma. *Tropical xanthoma* means juxta articular nodes which have been described on page 103 An interesting phenomenon is the so-called "xanthoma stage" in kala azar which resembles multiple tuberous xanthoma

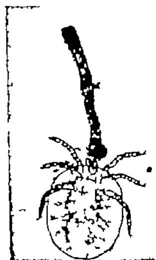
Xeroderma simplex occurs symptomatically and comparatively

often, in the tropics, in leprosy pellagra and volvulosis (Cf *crazy pavement dermatitis*)

Of *xeroderma pigmentosum* Fig 143 gives a distinctly clear example.

Zoonoses Of these, *scabies* is the most important representative. It is often complicated by pyoderma, with the result that it can no longer be recognized as scabies. A detailed chapter on the subject by BEEK appears in this book. See also batata.

"Gale des céréales" which occurs semi-epidemically in many seaports,



144 Trombicula batatas, larva with histosipho.
(Van Thiel–Leyden)

is characterized by a widespread, itching and sometimes febrile papulo-vesicular rash, localized chiefly on the back. It might put one in mind of a strongly pronounced prickly heat or of scabies It is caused by Pediculoides ventricosus (NEWPORT 1850). Pediculoides is actually a parasite of the larva of Lepidoptera, that lives in wheat or other grain (*cf* cotton seed dermatitis and SCHAMBERG s disease), and does not attack man unless these Lepidoptera are absent.

Body lice were formerly unknown in Indonesia (or at any rate not recognized as such) Not until the Japanese occupation were they

frequently seen. The first case was sent us at the hospital of the P O W camp with the diagnosis of phthiriasis The lice, however, were of the oblong body louse type, and their eggs were also found in the men s clothes This pest eventually spread rapidly In the P O W camps in Indonesia the body lice did not transmit any infectious diseases rickettsioses remained limited to rare cases and despite the occurrence of shop typhus there were never any secondary cases of this disease, which surely argues that it is improbable that epi demic spotted fever is caused by murine typhus through the passage



145 Conglomerate of Trombicula larvae on the scrotum.
(L en Thiel-Leyden)

of lice as is sometimes assumed in the case of Tabardillo (personal communication by DINGER) What the lice (not the lack of vitamins) did cause on the other hand, was the intense itch that vanished as if by magic as soon as the clothes had been boiled The violence of the itch is not proportional to the number of lice, because only a few lice are capable of setting up a very irritating pruritus.

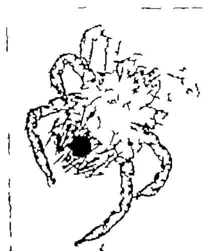
An older and better known tormentor in the tropics is the *merutu* or *mampirre* a tiny ceratopogon midge which can even pass through the meshes of the mosquito net. It causes itching and urticaria, and as a result, pyoderma, but does not, it appears transmit infectious disease

In Surinam, the *patatta luise* is the larva of Trombiculum flui and T. Vanommereni is found in the grass. Together with T. helleri (absent, or very rare, in Surinam) it belongs to the T. batatas group



146. A minute tormentor of the tropics, which even passes through the meshes of the mosquito net, causing a burning itch: the midge ceretopogon called punky, mampiras, merutuh. It is not definitely proved that it does not transmit acantho-cheilonema or fil. ozzardi.

(Van Thiel–Leyden)



147. This thrombicula batatas derives his name from the fact that it preferably attacks whites (whose nickname is "patat" in Surinam).

(Van Thiel–Leyden)

(LINNAEUS) (i.e. T. flui). BRUMPT distinguishes between Leptus batatas, the "bête rouge" of the Antilles, and T. flui and T. vanommeri.[1] The batata louse is also found on chickens and lizards. It is open to question whether it infests precisely (and exclusively) the batata plant, a supposition which, indeed, was contradicted by BONNE. VAN THIEL and VAN OOMMEREN on the other hand found the T. flui in the so-called "garter-plants" (leguminous Vigna sinensis); these authors assume that the name "batata louse" derives from the fact that the insect for preference attacks whites (whose nickname is "pataten"). Trombiculae *appear in huge swarms towards the end of the dry season, when the* great rains begin. The insects attack animals and humans walking through the grass, and attach themselves to the victim's skin. When the larva is removed from the skin, a tiny tube is seen on its head,



148. Trombicula-larvae under the epidermis of the praeputium.
(Van Thiel–Leyden)

called stylostoma or histosipho, and composed of necrotic tissue of the victim (or host, sometimes synonymous) and soaked thrombicula saliva. The mechanism has been described by VAN THIEL and VAN OOMMEREN in the Acta Leidensia (1940). In the same article these authors also reported the occurrence of trombiculae under the skin and in the prepuce. The itch and urticaria caused by the secreted toxins appear to be followed by some degree of immunity, as fewer or no complaints are found among people who have lived in the tropics for a long time, but only among newly arrived white immigrants.

[1] Leptus japa lives in the upland plains of Peru. Microtrombidium Wichmanni is found – under the name "*Gonone*" – in North Celebes. T. americana is synonymous with Sarcopsylla. T. brasiliensis, or *Vampire*, lives in Brazil.

Trombicula akamushi (= "red insect") or *kedani* and *Trombicula deliensis* are more dangerous for they are the cause of the so-called "kedani fever" or scrub typhus ("tsutsugamushi"), which is dealt with in more detail in the chapter on rickettsioses

A less-known zoonosis is the Mexican *Nunez Andrade disease* a trombidiasis caused by Neoschoengastia nunezi This condition reveals pruritus, haemorrhages, pustules and umbilicated papules.



149 Alfurian women (Indonesia) delousing each other.
(Dr Broen-Trop Inst., Amsterdam)

Bed-bugs (*i.e.* Cimex lectularius and (more frequent in the tropics) Cimex rotundatus), cause no infectious diseases, but they cause itching, and, in consequence, a dermatosis resembling prurigo nodularis Bed-bugs are harder to exterminate than body lice, since they infest not only the bed, but also the bed-frame and other furniture, the mosquito-net, the band around one's hat, the buckle of one's belt, books, etc. They emerge at night, and may travel dozens of yards to find their prey They are frightened at once of any light, and one need only strike a match to see them scamper away in all directions

The bed-bug has often been suspected of being an intermediate host in the infection of leprosy: further details concerning this point are given in the chapter on leprosy.

Siphunculina funicola is a tiny fly which is much attracted by ulcers (hence the Surinam name "sorro fre fre") and by inflamed eyes (hence also the name "eye" or "trachoma fly"). It is far from unlikely that this insect, in common with other chloropides (= oscinidae) such as *Hippelates* transmits the infection of tropical ulcer or of yaws. In Assam and Egypt, *Oscinus pallipes* probably transmits an epidemic conjunctivitis (? trachoma). See footnote page 13.

VORDERMAN (quoted from KAYSER) has described a case of urticaria with papules and bullae, to be attributed to the "smoet kalong" (Java) *i.e.* a beetle (Paederus peregrinus) which probably secretes a cantharidin-like fluid. According to ROUBAUD (quoted from KAYSER) different "caléoptères canthandiennes" are known also in Africa. PUJATTI described a seasonal vesicular dermatitis in South India caused by Paederus melampus, which leaves its habitat near water during the rains and is attracted by light. (Tropical Dis. Bull. 1950).

We may also mention here *mancha gangrenosa*, known in Chile, and caused by the bite of the house-spider Loxosceles laeta. The bite of the Surinam "bos-spin" (forest spider) can also set up symptoms similar to those due to the scorpion's sting.

Jelly-fish, e.g. the mediterranean Rhizostoma pullini when they touch a bather's skin,[1] may set up a violent *dermatitis medusica*. The "benang benang" (Physalia utriculus, of the order siphonophora (cited from KAYSER) is the most notorious in Indonesia. The bather, without in any way noticing the jelly fish, suddenly feels a violent burning pain, as if he has touched a red-hot plate. On leaving the water, the skin often shows nothing particular, but in some cases there is fairly serious erythema, either with or without oedema or even haemorrhage. In many cases the pain soon passes, but cases have also been described which were accompanied by dyspnoea, anorexia and general morbid symptoms. There are two poisons of which the one, *thalassin*, causes the local irritation, and the other *congestin* causes the respiratory symptoms (DOSTROVSKY in Hare

1 Should not be confused with swimmers' itch or seabathers eruption (*q.v.*)

fish Journal, 1935). Dermatitis due to the hairs of moths called *papillonitis* has occasionally been reported, for example by LE GAC, LAGARDE and MULET (Bull Soc. Path Exot., 1950) Attracted by strong light hundreds of moths *(anaphe venenata)* pestered the Europeans living in French Equatorial Africa. The natives escaped from the dermatitis, probably because they used oil lanterns.

Venereal diseases Although this work does not contain a special section dealing with venereal disease, some venereal conditions are described in a separate chapter

In some tropical areas the frequency of chancroid may be high It



150 Jelly fish dermatitis medusica.
(Doctrow by Jerusalem)

may even occur epidemically as I experienced in Java in the beginning of the war. Diagnosis is made by the identification of Haemophilus ducreyi and by skin tests with the vaccine. The ulcer should be distinguished from primary syphilis, yaws, and leishmaniasis but the main thing is to remember that, even when H ducreyi is found a mixed infection with syphilis may come to light (a) when the ulcer opens again, (b) when the edges become firm, and (c) when the blood tests for syphilis (which should be done after two months in all cases) become positive WILLCOX reported evidence of widespread chancroid

in some parts of Africa (Southern Rhodesia, Gold Coast) (Bull. World Health Org. 1951). In this connection, BEHÇET's syndrome, although not a venereal but a genital disease, may be mentioned. It comprises aphthosis of the mouth and vulva and conjunctivitis. The aetiology is still obscure.

We conclude this chapter with a few remarks concerning the **treatment of skin diseases in the tropics**, at any rate in so far as it differs fundamentally from that in Europe. This applies most particularly to the wholesale treatment of epidemic dermatoses such as yaws. HACKETT – in chapter 7 – states that, although it may be attempted to give each individual patient adequate treatment, this method will usually fail to achieve the desired result, and that it is better, therefore, to make an effort to clear an entire district of the disease by reducing the chances of infection. To this end, as large a number of patients as possible would receive some injections; only after this should individual therapy be proceeded with. For wholesale treatment, the most practical use can be made of travelling equipment. This principle, however, should not be confused with the "out-patients boats" or automobiles which call at a dessa for a few days only and distribute quinine, ointments and other medicaments. By this method one may admittedly succeed in getting rid of a large quantity of medicines (and money), but it is open to question whether it facilitates the proper treatment of a single case of malaria, skin disease, etc.

It may be possible to achieve some results by means of ambulant clinics stopping in a place for a few days only for the purpose of vaccination against smallpox, etc. or to prevent yaws from spreading, but this is not therapy. Such ambulant clinics, therefore, should really pitch their tents for a longer period.

The follow up of patients (we think here also of venereal diseases) in these vast areas, where one settlement is often hundreds of miles away from the next, and where there is no such thing as a population register, is usually so difficult as to be foredoomed to failure. For this reason, wholesale treatment by reducing the chances of infection is the opposite number in the tropics of complete individual therapy in Europe and America, where the patient need not be a needle in a haystack. The difficulties attending epidemiological work were already referred to briefly on page 34. I might point out here that the expres

tion "not yet" frequently heard all over Asia in answer to the question whether the patient has had a given disease in before, does not imply that the population regards the disease in question as quite the usual thing, since "not yet" is merely a polite form of "no" customary among Asiatics

In real dermatotherapy—in so far as it differs in the tropics from that in Europe—treatment with *ointments* occupies a prominent place. In many cases fatty salves are not well tolerated in the tropics, for which reason one will, sooner than in Europe, have recourse to pastes, lotions and cold creams although their action is less deeply effective.

When dealing with a female patient it is advisable to inquire



151 Not late yaws but arsenical dermatitis following *treatment* of yaws!

whether she uses cold cream, and if so what brand, when the same substance may be used as a base of the ointment. Since the patient's greatest problem is not how to get the ointment on, but how to get it off it is also most important to give him or her the necessary instructions to this end in order to prevent the use of water petrol or soap Many doctors, indeed, are supposed to have failed (and many ointments, to have made things worse), because the dermatosis was prolonged either by insufficient application or by inadequate removal or by the patient's own therapeutic intervention.

Compresses as applied in dermatotherapy (and definitely in the

tropics) should nearly always be made without impermeable covering which cause hot fomentation. There is one remedy which deserves particular mention the wearisomely popular salicyl lotion the panacea of the tropics. It is used with some alacrity for eczemas, but only in parasitogenic eczemas it has any useful effect being usually harmful in most other eczemas. One often sees cases in which, once the parasitic eczema is cured, a salicyl irritation is taken for a relapse of the original eczema is again treated with salicyl lotion, and in the long run turns into a chronic and sometimes lichenified eczema Fungous diseases too are best treated for say one week with 1–2 % salicyl or resorcinol spirits, after which this therapy is stopped for a week or two and resumed for another week if necessary A more modern therapy for fungous disease is described in the appropriate section.

Lotions (especially calamine lotion) are as a rule, applied with good effect in prickly heat but soap is generally used far too generously in the tropics by most people. Different factories, large and small, produce sharp smelling medicinal soaps (carbolic soap) that often have an irritating action, just too weak to cause a distinct dermatitis and just strong enough to produce a chronic pruritus. *Medicinal soaps are good only for the healthy skin*

X ray therapy should always be applied with a great deal of extra care It sooner produces pigmentations and erythema too may appear with lower doses than in Europe. For this reason X ray epilation is by European standards risky URBACH and REISS state that X rays produce dark pigmentation in the wealthy Chinese owing to their photosensitizing soya nourishment (The poor Chinaman, on the other hand gets his— be it different—dermal discoloration through xerosis due to vitamin A deficiency (MU and PILLAT)

I would here call attention to a peculiar factor in the therapy of skin disease Although not unknown, this factor is not given sufficient attention because it has no name Names after all, are needed if we are to classify our diseases methods and concepts I propose to call the concept in question *therapeutic panic* It happens very often that a patient gets into a kind of panic when the treatment does not seem to be making any headway He may not jump out of the window as one might expect in a case of panic but he no longer sees the way out and

the long road he has to travel The most dangerous aspect of this panic—and this is far from rare—is that the physician, too gets panicky *i.e.* loses sight of the "main entrance the main exit, and even the side entrances The patient catches at the most improbable ideas and may provoke the physician to determining his thyroid function, giving him a blood test, prescribing vitamins or calcium, etc., which are just as inadequate as tonsillectomy or appendectomy would be. The patient, in short, loses his head, and what he asks for is nothing more or less than *pseudo-scientific intervention in scientific work*. In such a case of therapeutic panic the physician should on no account permit himself to be put out of countenance, but remain firm and steadfast as would be expected of any leader when a panic breaks out.

Since the comparative lack of medical and specialist assistance in the tropics sooner leads patients to attempt their own treatment (and also, therefore, to try to "help the doctor on"), the danger of therapeutic panic is greater in those climates than in countries with stronger scientific bulwarks The physician posted to a remote tropical station should therefore, if he is to act in the capacity of a strong advanced scientific warden, provide himself with the best literature. If, on the other hand, he derives his therapy from the many existing markedly one sided commercial pamphlets he will, in cases of therapeutic panic, resort to the wrong treatment, and cast petrol on the fire instead of water or sand.

Therapeutics which vacillates between science and quackery—and which exists ubiquitously—has a happy hunting ground especially in the remote tropical regions. For this reason, more knowledge, and, more particularly more self knowledge must be expected of the tropical physician, the critical eye of rivalry" being often absent. That physician will be hopelessly lost whose maxim it is that every Chinaman (*i.e.* rich Chinaman) can do with a little arsenic or penicillin, and who at the patient's request for some strong medicine, gives him suggestive calcium injections hormones and series of vitamines in so-called "courses of treatment" Such a psychotherapy" particularly anaesthetizes the physician's conscience and undermines both medical authority and bona fide science. It encourages quackery which, now behind the mask of pseudo-science now openly in the

form of magic, finds a ready market for all sorts of herbs said to possess medicinal properties

With the argument—so familiar to us—that so many kinds of herbs are already being used in medical science which were once derived from native therapeutics, and that, after all, tropical diseases ought to be treated with tropical herbs, the patient is attempted to vindicate the wisdom of the dukuns the shinshes tabibs and wiesle men. And he forgets that the ointment will not help him unless he smears it on, or who expects that a single application will, as if by a conjurer's trick immediately produce a healthy skin, wanders from one doctor, specialist or pseudo-specialist to the next

Truly it is especially in the tropics that the maxim is valid *The modern physician's magic is knowledge*

CHAPTER 2

SOME ASPECTS PECULIAR TO THE PRACTICE OF DERMATOLOGY AMONG CHILDREN IN THE TROPICS

D. P. R. KEIZER – Hilversum
A. GIRDWOOD FERGUSSON – Glasgow
J. LAPIERRE – Paris
V. A. R. MONTENY – Kilo Moto (Belgian Congo)

For the doctor engaged in paediatric practice in tropical areas, a profound knowledge of the common diseases of the skin is of primary importance. Each little patient usually presents a cumulative diagnostic problem, and it must be in the first place appreciated that a simple diagnosis of "pyoderma" is of no significance. A search in infective conditions of the skin in tropical lands must be directed towards isolation of the original infecting agent which may be one of such widely differing factors as the Sarcoptes hominis, the spirochaete of yaws or the diphtheria bacillus. Then and only then can rational and specific treatment of a great many cases of apparently simple pyoderma be instituted and carried to a successful conclusion.

PYODERMA

Cases of severe pus-coccal infection (*impetigo, ecthyma, infectious eczematoid dermatitis*, etc.) are the conditions most commonly seen among infants and children in tropical areas, since climatic factors in the form of heat and humidity essentially favour their development. Such diseases as indicated above, are seldom primarily due to staphylococcal and streptococcal infection but are usually examples of secondarily infected scabies or yaws or of primary infections of the skin by the KLEBS-LOEFFLER bacillus. Primary cases of *pyoderma abscedens et suffodiens* (HOFFMANN) affecting the scalp are, however, not uncommon. These present the familiar clinical picture of phlegmon-

ous swelling from which pus rich in staphylococci escapes by way of multiple sinuses *Dermatitis gangraenosa infantum* is sometimes seen in



152. "Impetigo" of cutaneous diphtheria.
(Le Coulant and Sourreil–Bordeaux)

marasmic infants and children It is also encountered as a complication of severe varicella, where the "pocks" have become secondarily infected by Ps aeruginosa.



153 F tal case of tropical ulcer
(Radhakr– 1 nerp)

Tropical ulcer still generally considered to be due to infection of skin abrasions by the symbiotic spirochaete and fusiform bacillus of VINCENT presents the usual picture of severe phagedaenic sloughing of the skin and subcutaneous tissue, the lower limbs being the areas most commonly involved. Pemphigus contagiosus, which is merely a severe and often widespread form of the bullous impetigo of temperate zones is a common disease among children in the tropics It frequently complicates miliaria rubra (*q.v.*) and occurs most often among the offspring of European residents since native children do not tend to suffer so much or so severely from the prodromal condition.

Noma or gangrenous stomatitis which may complicate scarlet fever measles, etc. is quite frequently met with. The Madagascar noma, which is perhaps identical with oral tropical ulcer is described in chapter 17 (See also Fig 108)

CUTANEOUS DIPHTHERIA

Native children seldom suffer from nasal and faucial diphtheria but cutaneous diphtheritic states are rife among indigenous populations This incidence is in marked contrast to that obtaining among European infants and children living in the tropics who commonly contract nasofaucial infection and only develop cutaneous involvement under conditions of malnutrition and lack of elementary hygiene such as were encountered in prison camps during the recent Japanese occupation of a large part of the Far East.

SCHICK *testing* of native children (SMITH) revealed a very high percentage of negative results among those over five years of age. It is surmised that this immunity may be acquired by low grade infection, and that the frequency of cutaneous diphtheria among natives may explain this

BIBERSTEIN gives the following classification of cutaneous diphtheria

I *Epidermocutaneous form*—including pustulous impetiginous ecthymiform and eczematous types.

II *Cutaneous subcutaneous and deeper types*

III *Diphtheritic paronychia* (panaritium subunguale)

Of these group I would seem to be that most frequently encounter

ed. The impetiginous form is often noted to involve the skin of the chest abdomen, face and hairy scalp while the ecthymatous type is usually seen on that of the legs where it may closely resemble either simple coccal ecthyma or tropical ulcer The eczematous form is



154 Secondary yaws and keloid tattoo.
(Jelliffe–Ibadan)

clinically very similar to intertrigo and involves body folds the deeper examples present as globular infiltrative lesions which may closely resemble cutaneous gummata There may also be involvement of conjunctivae and of oral and genital mucosae.

The importance of careful bacteriological examination of all cases of pyoderma encountered under tropical conditions cannot be too strongly emphasized since it is often impossible to rule out cutaneous diphtheria on simple clinical inspection. A pyoderma which shows little improvement with simple antiseptic treatment calls for speedy investigation directed towards the possible presence of a graver type of



155 Spina ventosa due to tertiary yaws. N.B. deformation of the wrist.
(Wolff Paramaribo)

infection than would be caused by pyococci. (*vide* chapter 18).

YAWS

This is a common disease among native infants and children in whom it follows the usual course. The so-called "mother yaw" at the site of infection, is seldom identified as such. When first seen, the little



156 The sabre or boomerang leg is often said to be due to yaws but according to H   KETT this problem has not yet been worked out Perhaps rickets is   predisposing factor



157 I at   s   resistant to arsenicals and cured by penicillin.
(Wolff Paramaribo)

patients commonly reveal the typical framboesiform lesions often ulcerative or covered by crusts on account of superimposed pus-coccal infection. Cases presenting tertiary yaws are also not uncommon at early ages.

CONGENITAL SYPHILIS

The symptomatology does not differ in any way from that seen in temperate zones apart from the occasional appearance of the rare circinate secondary syphilids which seem to occur almost entirely among inhabitants of tropical and subtropical regions particularly African negroes. Syphilis in all its forms is, of course, rife among



158 Njovera or non-venereal syphilis the external lesions are often confused with those from yaws or pyogenic angular stomatitis or perlèche from vitamin deficiency See also Fig 243

([illegible]—London)

the peoples of Africa, South America and the Far East, more especially India and China. Congenital syphilis should be distinguished from non-venereal infantile syphilis, called bejel, njovera etc. (See chapter 6)

TUBERCULOSIS OF THE SKIN

The tuberculous disorders of the skin differ little among native and European children. *Lichen scrofulosorum* is occasionally seen as a complication of systemic tuberculosis. *Erythema nodosum* is probably more often seen in association with systemic mycoses, lepra, the dysenteries

and sulphonamide drug hypersensitivity than in tuberculous subjects *Granuloma annulare* is a comparative rarity In the tropics what appears to be granuloma annulare is often a circinate syphilide or creeping eruption (*q.v.*)

LEPROSY

As this subject is extensively dealt with elsewhere in this book, it is sufficient to say here that there would appear to be general agreement that children under five years of age are most susceptible to infection. Skin to skin contact with open (lepromatous) cases is thought to be the most likely route of infection as regards infants and children. In this book Simons has again drawn attention to the fact that an insect vector may exist.

CUTANEOUS LEISHMANIASIS

A not uncommon disease among children, it is of interest to note that this condition is unknown in Central Africa despite its widespread endemicity in other warm parts of the globe. This subject has been fully dealt with in chapters 11 and 12.

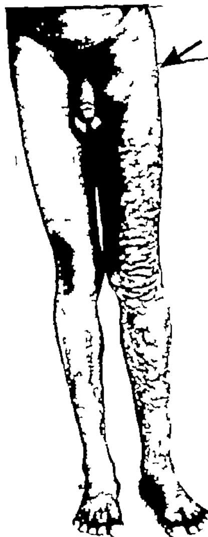
FUNGOUS DISEASES OF THE SKIN

Ringworm of all types including favus is common among children in tropical lands that of the scalp and glabrous skin predominating The infecting agent in the majority of cases of scalp ringworm in the Far East is the animal microsporon (M. lanosum). Controversy continues as to whether the condition know in South Africa as Witkop is of syphilitic or favic origin. Since it may be connected with *Kaalkop* (*i.e* bald scalp) we are in favour of a fungous disease

Barefooted native children seem to suffer less from epidermophytosis and the pyococcal complications of eczematoid ringworm of the feet than do their European brothers and sisters whether the latter are resident in tropical or temperate zones The sole of the native foot is horny and thickened due to exposure and intermittent pressure, and the relatively alkaline medium provided by excessive sweat secretion, which offers a very suitable medium for pyogenic organisms, is not the important factor in aetiology which obtains in children who constantly wear foot coverings



160 Elephantiasis scroti from filariasis Bancrofti in a 9 year old boy
(Lampe–Trinidad)



159 Chronic onchodermatitis with microfilariae in the skin lesions in a 15 year old boy
(Jelliffe–Ibadan)

The systemic mycoses and other fungous diseases (*e g* piedra, tinea imbricata and nocardiosis cutis) which are more or less endemic in tropical and subtropical areas will be dealt with in detail in another chapter All occur in children as well as in adults

complicating condition in severe cases of measles is noma or cancrum oris now rarely seen in Europe. (See chapter 17).

Rubella seems to be less frequently encountered than in temperate climates but many cases of this affection and of glandular fever are probably mistaken for dengue. The same may be said of *erythema infectiosum* (Fifth disease) and *roseola infantum*. *Erythema epidemicum arthriticum* whether due to infection by spirochaeta morsus muris or streptobacillus moniliformis is frequently seen in lands in which



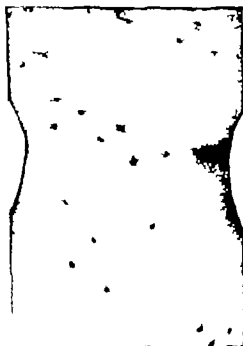
163 Measles in 4 year old Nigerian boy. Note edema and photophobia. *(Jelliffe–Ibadan)*

contamination of milk and the presence in dwellings of multitudes of rats and mice are frequent. In this last connection it must be stressed that a positive WASSERMANN test is by no means proof of luetic or yaws infection in the tropics

Erythema toxicum neonatorum (LEINER) and *dermatitis exfoliativa infantum* (RITTER) are often seen in newly born native infants

The reversible diencephalic syndrome known as *acrodynia* (SWIFT FEER *disease*) presents its familiar skin picture of intense palmar and

plantar erythema and a morbilliform eruption on the trunk and limbs. The fact that mercury in medicinal preparations would appear to play a part in aetiology gives rise to interesting problems in the tropics. It is not advisable to prescribe calomel as an aperient in treatment of bowel infestations and other irritative conditions of the alimentary tract while even local application of mercurial lotions and



164 Varicelliform syphilis all lesions [at] the same stage.
(Carol–Amsterdam)

salves in the treatment of cutaneous infections may be dangerous. Salt depletion may of course be important in this connection also.

Erythema exudativum multiforme until recently a rare affection during childhood in the tropics, is now becoming more common in all its forms (also erythema nodosum and erythema scarlatiniforme) owing to the increasing use of sulphonamides, penicillin, quinine and



165 V ricella or chicken pox "Scars of ark t sizes Note different stages w th or witho t umbilication.

(Siemens–Leyden)



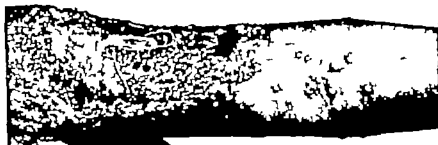
166 Varic llif rm cut neous diphtheria

(Le Coulant and Sourreil Bordeaux)

mepacrine in the treatment of general and local infections of various kinds and of sedatives for the control of epilepsy. Urticarial eruptions are common among native children, aetiological factors being physical (heat and light) chemical (vaccines, sera, drugs) and parasitic (exogenous and endogenous infestations by parasitic fungi and worms).

DISEASES DUE TO VIRUS INFECTION

Smallpox presents a considerable problem in some areas of the Far East, particularly India and China, and is also very prevalent in the Middle East and in North Africa. In Indonesia, the disease has been in general very efficiently controlled by the Dutch authorities by a



167 Satellite vaccinia following vaccination of a Javanese child. Note the umbilication.

(Simons—Amsterdam)

system of mass vaccination. It must be said, however, that one untoward result of this mass prophylaxis in Indonesia has been an increase in the incidence of generalised *vaccinia* (and probably also of Kaposi's varicelliform eruption). This has been due to out-patient inoculation often carried out under local conditions of poor hygiene and in many cases among children suffering from pre-existing skin disease. Postvaccination encephalitis is discussed in the chapter dealing with variola.

Cases of *varicella* tend to be severe and to become quickly secondarily infected by pyococci, a common and disfiguring complication being as noted above dermatitis gangraenosa infantum due to superimposed

infection by Ps aeruginosa As in all parts of the globe, association of childhood cases with adult herpes zoster is often noted

Herpes simplex (*febrilis*) is frequently seen in association with



168 Herpes simplex in a 10 year old Dutch child in Jakarta. *(Simons—Amsterdam)*

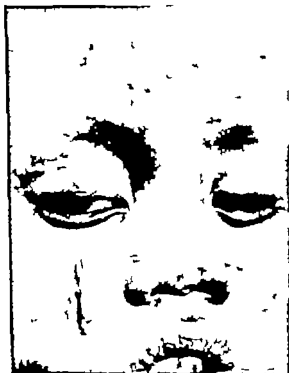
febrile illnesses and genital examples are especially common among Africans owing to local irritation in association with certain tribal customs

AVITAMINOSES

Vitamin and other food-deficiency diseases are common in tropical lands *even in the absence of famine* and in times of peace. Their prevalence is usually due to neglect of principles in the regulation of childrens diets and also to religious opinions as to what foods should and should not be consumed To some extent also there may be geographical reasons for the paucity of food factors of certain kinds in the diet of indigenous populations, since the native tends in the absence of knowledge of modern methods of cultivation, to sow the crops which he can most easily grow and this without regard to their pure food value Further the increasing use of the sulphonamides and penicillin in the treatment of systemic diseases particularly the

dysenteries, may be a potent factor in disturbing the natural synthesis of certain vitamin complexes in the gut.

Avitaminosis A is extremely common in Asia and its symptomatology includes ocular as well as cutaneous eruptions of the phrynoderma type, although an upset in fatty acid metabolism



169 Early eruption of smallpox in a 3 year old Nigerian child
(Jelliffe–Ibadan)

may also be an important aetiological factor in such cases. One of us (A G F) observed phrynoderma in association with sprue in Indian children, although such cases are seldom seen. *Vitamin-B_1 deficiency* is never the sole cause of skin disease in childhood.

Deficiency of the B-complex may be apparently single but is more

often multiple, with cardinal symptomatology pointing to absence or attenuation of one of its factors. It often coexists with other vitamin deficiencies, a good example being dermo-beri beri (CASTELLANI) which presents a mixed picture of B_1 deficiency and pellagra.

Ariboflavinosis shows the well known quatrad of cheilosis, perleche, facial seborrhoeic eczema" and circumcorneal vascularisation. Nicotinamide deficiency presents the usual picture of pellagra, with its associated desquamating erythema of the skin of the hands, face



170 Oedema of the face and ascites from B_1-avitaminosis; the legs are not oedematous.

(Simons, Amsterdam)

and feet passing into a stage of intense sepia-coloured pigmentation which is striking even in dark skinned subjects. Many children who passed part of the recent war in Japanese internment camps were noted to have a serious patchy alopecia of the occiput and posterior hair margin, which recalled the "plucked fowl" appearance of laboratory animals suffering from experimental inositol deficiency.

It seems almost certain that the condition known in different areas of Africa, *kwa hiorkor* (Nigeria), *m'buaki* (Congo) and *dibobe* (Kasai) is simply a variant of the pellagra syndrome with associated hypo-



171 Sensitivity to light in pellagra.

(Hackett–London)



172. Phrynoderma due to Vitamin-A deficiency

(Fasal–San Francisco)

proteinaemia and amino-acid deficiency. Any breakdown in breast feeding by native mothers may bring about a state of grave infantile malnutrition, since properly regulated and controlled artificial feeding is difficult if not impossible to carry out among primitive peoples. The disease is characterised by a reddish tinge of the entire skin, a 'rusty' appearance of the hair, lower limb oedema and, if anaemia is present, pallor of the mucosae. In some cases there may be widespread bullous eruptions, stomatitis and cheilosis.

Vitamin C and D deficiency syndromes are uncommon among native

173 Kwashiorkor, mbwaki or diloba, most probably a variant of pellagra. Note oedema and "paint flake" appearance.

(Jelliffe–Ibadan)

children but drenching sweating associated with rickets is often seen and may provide a suitable soil for complicating milliaria and pyoderma.

MISCELLANEOUS DISEASES

Eczema infantum is almost unknown in the tropics: the reason may be that nearly all native infants are breast fed and that their mothers' diet may be lacking in many allergenic factors present in that of European women.

Strophulus (which the Leyden clinic considers to be a virus disease)

(BOTTER) is not common in the tropics and for that reason natives do not become immune this may account for outbreaks of strophulus among Indonesian adults after arrival in the Netherlands.

Anomalies of pigmentation are commonly seen and include Mongolian spots, melanin lines" xanthochromia cutis vitiligo and albinismus. Mongolian spots are generally small in size and situated in the usual lower sacral position but occasionally the pigmentation is found to involve the entire skin of the back, or alternatively the macule may be atypically situated on the bridge of the nose. Such anomalies commonly disappear without treatment at the age of two years but



174 Strophulus in a Javanese adult after arrival in Holland.
(Siemens Leyden)

are sometimes more persistent. Another form of pigmentation, probably atavistic, is represented by the *melanin line* in the gums of some coloured children. It is important that this should not be confused with gum pigmentation due to metallic poisoning

Xanthochromia cutis is exemplified by carotinaemia, a generalised yellow pigmentation caused by excessive ingestion of oranges, squashes, mangoes melons and tomatoes. Peculiar red and blue macules seen on the abdominal skin of Chinese and Javanese children may be caused by burning in an attempt to cure internal pains or to expel "evil spirits"

Parasitic achromia undoubtedly exists commonly presenting as a sequela of fungus infestations and due either to disturbance of pigmentation by scale formation, or to a depigmentary action of the fungus itself *Vitiligo* and *albinismus* together with the above, are chiefly important in that sufferers may be shunned by their playmates under a mistaken impression that the disease is leprotic, but may also cause considerable illness owing to the tendency of the achromic areas to react to strong sunlight with a vesicular dermatitis.

Among hypertrophic states, *keloid* is common among coloured children and is to be found with frequency among those of other dark



175 Haemangioma in a Chinese child from M lakka
(Fasal—San Francisco)

skinned races The reason for the increased incidence of this peculiar form of scarring among inhabitants of tropical lands remains conjectural

Kerato cc often fissured and painful but showing comparatively little secondary infection by pyogenic organisms commonly involve the soles of native children.

The condition known as *verruga peruana* (Peruvian wart) is often seen in both infants and children and is chiefly endemic in the inland parts of Peru The mild form of the condition is the rule in young persons in whom there are at first miliary papules on the skin of the

face and forearms and later nodular lesions which chiefly involve the extensor aspects of joints and sometimes the oral and genital mucosae. These later excrescences are warty and tend to bleed easily on slight trauma in many instances they closely resemble pyogenic granulomata.



176 Artefacta in a 12 year old girl.
(Simons–Amsterdam)

There is an associated microcytic anaemia one attack appears to confer lifelong immunity

Warts and *molluscum contagiosum* are common in the tropics.

Atrophic conditions of the skin (*e g* congenital ectodermal defect and monilethrix) are seen among both European and native children in the tropics but probably more often among the latter The preva lence of marital consanguinity among coloured peoples has not a little to do with this higher incidence of ecto-mesodermal dysplasias.

Psoriasis is not uncommon among children in tropical and sub-subtropical areas (FERGUSSON, SIMONS) and its chief importance lies, as in the case of depigmentary states, in the fact that its eruption may be mistaken for that of HANSEN s disease by the untutored native with unfortunate results for the sufferers Furthermore, secondary pyococcal infection of the lesions, particularly those situated in body folds may cause a considerable symptomatology which is normally lacking in cases occurring in temperate regions

Scaly skin eruptions of lichenoid character recalling the so-called tropical lichenoid dermatitis of the recent war in the East, are beginning to be seen in children in association with the atabrin prophylactic treatment of malaria. Ichthyosis may also occur in tropical races. One who is not familiar with it may regard the child as being dirty Confusion may also arise with regard to vitamin deficiency and even to tinea imbricata.

Miliaria rubra is a disease of comparatively mild nature among native children it occurs more commonly among fair skinned infants



177 Mollusca contagiosa in Malayan boy
(Fasal Sen I [illegible])

and children residing in hot climates Though in itself an irritating disease which is causal in severe cases of grave complications such as tropical anhidrosis and thermal fever its complication by pyococcal infection with the production of superimposed and secondary bullous impetigo constitutes the hazard most usually encountered

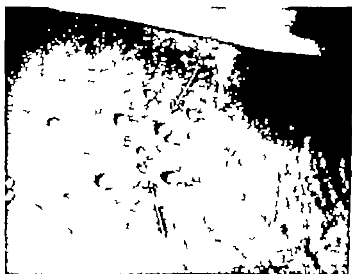
It is thus clear that the study of diseases of the skin affecting infants and children in warm climates is of fascinating interest, constituting

a field of diagnosis which abounds in intricacies and pitfalls and demands considerable skill in observation. Not the least of the difficulties encountered is that of recognition of common lesions on a dark skin. The ability to assess the nature of lesions under such conditions can only be acquired by continual inspection and experience

One remark about a condition generally regarded as venereal, *i.e.* vulvovaginitis in young girls In many cases this condition turns out to be non-gonorrhoeal Girls complaining of pruritis vulvae and fluor albus should sooner be suspected of oxyuriasis, a diagnosis which, however, is often arrived at only after repeated examination.

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CHAPTER 3

PIGMENTARY DISORDERS

S. WILLIAM BECKER
Chicago

MELANOSIS SOLARIS

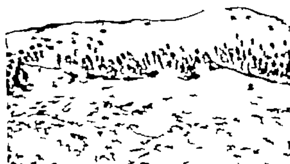
Suntan is common in the tropics because of the intensity of the sun's rays. The colour is brown because the pigment is predominantly in the epidermis. While it is most noticeable on lighter skins, even the darkest Negro shows further darkening on portions of the body exposed to the sun as contrasted to covered areas. Tanning is caused by two distinct processes, known as indirect and direct, which depend on rays of different wave lengths.

Indirect pigmentation results from enzymatic activity in a sheet of melanoblasts at the epidermo-dermal junction (Fig. 178), caused by erythema producing ultraviolet irradiation (under 320 mm). According to EDWARDS and DUNTLEY, hyperaemia in Boston in August at noontime is pronounced in two hours, with maximum in 11 hours. Melanin is apparent in two days, with maximum on the nineteenth day. Melanosis starts to diminish in one month, and pigmentation is normal in nine and one half months. Melanosis produced by ultraviolet therapy of vitiligo is shown in Fig. 179.

Direct pigmentation, according to HENSCHKE and SCHULZE, results from oxidation of preformed melanin by wave lengths from 460 mm to 300 mm acting from two minutes to one and one half hours. Oxidized melanin is darker in colour than reduced melanin.

PHOTOSENSITIZATION

Various substances sensitize the skin to ultraviolet irradiation. Among them are trypaflavine and other acridine derivatives, often



178 Addison's disease. A sheet of melanoblasts lines the basal layer and sends dendrites outward between the palisade basal cells. (Paraffin-dopa reaction carmine counter stain).
(Becker and Obermayer Modern Dermatology and Syphilology Lippincott Company Philadelphia, 1947)



179 Melanosis solare in islands of returning pigment in patches of vitiligo in nat[illegible] of India.

given intravenously sulfonamides, usually administered by mouth coal tar and pitch, which are contacted externally either in industry or as local medicaments and extracts of various plants, to which the

skin is exposed, either in gardening or accidentally. Among them are European agrimony (Agrimonia eupatoria), the common fig (Ficus carica), the common rue (Ruta graveolens), fraxinella (Dictamnus fraxinella), the "gas plant" (Dictamnus albus), cow parsnip (Heracleum sphondylium), garden parsnip, parsley, celery, wild carrot, angelica, lime, Indian lemon grass and others. KLABER called sensitization to plants *phytophotosensitization*.

The various plant extracts, commonly containing volatile oils, *must be rubbed into the skin*, after which the area must be exposed to ultraviolet irradiation between 310 and 370 mm. Common offenders are oil of bergamot, a constituent of Eau de Cologne which is often applied to the skin before sunbathing, and oil of Persian limes used for making



180 Berlock dermatitis of forearm.

limeade. Erythema and subsequent inflammation following such application and exposure to the sun is known as *Berlock (berloque) dermatitis*, which, in turn, is followed by melanosis (Fig. 180). Many persons do not notice the erythema at all and maintain that the hyperpigmentation was the original change. The photosensitizing substances are furocumarins according to KUSKE.

Photosensitization dermatitis is seen in pellagra, which is a nutritional disorder. The eruption is symmetrical and predominant on exposed surfaces, namely—the face, dorsal surface of the hands and the neck, including the "V" area. The dermatitis has its onset in early summer and is followed by hyperpigmentation. Treatment consists of a balanced diet, along with vitamin B components. Nicotinic acid or nicotinamide may be injected intravenously, given intramuscularly or

orally The dose for an adult is 500 to 1000 mg daily in divided doses of 50 to 100 mg Thiamine chloride, riboflavin and the B complex may also be useful, especially if the patient is an alcoholic.

CHLOASMA

The designation "chloasma" was formerly used for various melanotic disorders but is now used chiefly for a patchy melanosis, usually on the face (Fig 181) but sometimes seen on other portions of the body It tends to be persistent, and is aggravated by exposure to the sun. It is often seen first during pregnancy in which case it is called "chloasma



181 Chloasma
(Becker and Obermayer Modern Dermatology and Syphilology)

uterinum" CASTELLANI and CHALMERS state that such a disorder is common in Singhalese women. LOEWENTHAL states that it is of frequent occurrence in African Negro women, but careful inspection is necessary to verify its presence.

Chloasma is also seen in association with malaria and Kala-azar tropical sprue and, at times, in tuberculosis PIERS reported chloasma-like melanosis in three members of a Hindu family and states that Hindus are predisposed to such pigmentation. FINDLAY and BARNES have reported it in South Africa in porphyria (*q.v.*)

Chloasma bronzinum or *tropical mask (Castle)* is seen in natives and Europeans in India, Ceylon, the Malay states and other tropical countries. Part of the face or occasionally the whole face, neck and

chest show pigmentation resembling a black bronzine mask. The pigmented areas enlarge slowly the disorder is chronic and incurable, unless the person leaves the tropics. Prolonged stay in a temperate zone generally improves the disorder

MELANOSIS CALORICA

This disorder often reticulated (Fig 182) since it follows erythema ca loricum, is a brown pigmentation, seen in persons exposed to extreme heat as in stokers of furnaces DuBois mentioned the disorder in an



182 Melanosis calorica aft application of heat t abdomen
(Becker and Obermayer Modern Dermatology and Syphilology)

Algerian woman who kept an oven between the thighs. Such an oven i also used in Kashmir Kolb and Wlassics reported the disorder in a street vendor of hot roasted chestnuts

POST-INFLAMMATORY MELANOSIS

Because of the dark complexion of a majority of inhabitants of the tropics post inflammatory melanosis is very common. Simple irri tation, such as that following application of a cantharides plaster is followed by melanosis in the area. In members of the darkest races the preceding erythema often passes unnoticed, so that the hyper pigmentation is thought to be primary The involved area has a bluish or grayish hue shown by Loewenthal to be caused by deposit of

melanin in the dermis. The blue stage of pinta shows as abundant a deposit of melanin in the dermal chromatophores as I have ever seen in a benign condition. *Pinta* is a treponemal disease characterized first by inflammation, the so-called "*red phase*," which is followed by post inflammatory melanosis, the "*blue phase*," and still later by the *depigmented stage*.

It is sometimes possible to identify the original disorder by the distribution, as, for instance, the butterfly area across the nose and



183 Leukomelanoderma following exfoliative dermatitis caused by neoarsphenamine ("taches négatives").

cheeks in *lupus erythematosus* or repeated recurrence of *urticaria* followed by melanosis in the same sites, as in *fixed drug eruption*.

Manifestations of certain diseases are prone to be followed by melanotic macules, as, for instance, *secondary papular syphilis*, *lichen planus-like atabrine dermatitis*, *bismuth or gold dermatitis*. Ulcerative late syphilids leave atrophic scars with hyperpigmented borders. Erythemato-pigmented macules occur in lepromatous *lepra*, as do depigmented atrophic, anesthetic scars with hyperpigmented borders.

Exfoliative dermatitis from any cause may be followed by generalized melanosis or leukomelanoderma (Fig 183). Superficial lymph nodes often contain considerable melanin and lipoids.

INCONTINENTIA PIGMENTI

This designation is used for a systematized nevus first described by BARDACH. The pigmentation was studied by BLOCH and SULZBERGER, who gave it the above name. It has its onset, almost exclusively in female babies, a few days or weeks after birth, in the form of an inflammatory often papular or bullous eruption on the trunk, occasionally also on the extremities. After several weeks or months the inflammation recedes, giving place to post inflammatory melanosis in a bizarre, symmetrical pattern. Various developmental defects occur with the disorder such as hypodontia, retrolental fibrosis etc. As with all post inflammatory melanosis, the pigment fades out in a few years. This condition is also described in the following chapter

VAGABONDISM

This disorder follows long continued presence of body lice (Pediculus vestimentorum) It is characterized by generalized melanosis, more pronounced on covered areas associated with scratch marks, secondary infection and eczematization. The face and hands are usually free, although the buccal mucosa is sometimes pigmented. This finding associated with low blood pressure, suggests Addison's disease. The pigment persists for months after the body lice have been eliminated

RIEHL'S MELANOSIS

During the first World War RIEHL reported melanosis of the face and neck characterized by brownish gray colour (Fig 184) Involvement of exposed areas suggested photosensitization, possibly by substitute foods Microscopic section revealed much melanin in dermal chromatophores, but very little in the epidermis, thus accounting for the gray colour Other Austrian German, French and British authors soon reported the same disorder following application of substitute soap oils and ointments in addition to ingestion of substitute foods. CIVATTE and ELIASCHEFF called the disorder *poikiloderma*" but later CIVATTE stated that his patients were identical to those reported by RIEHL The buccal mucosa is only rarely pigmented. DEGRACIANSKY stated that the same disorder was frequent in France during the occupation from 1940 to 1944 when substitute materials including foods were again used. CORDERO reported RIEHL's melanosis in Argentina in persons using ochre or brown cosmetic powder from the same fac

tory Patch tests with the powder were positive in 70 per cent. of the patients. He believes that the dyes and perfumes are responsible Discontinuance of the powder was followed by cure in eight months. ARZT in 1947 stated that he had seen many persons (77 women and



184 RIEHL's melanosis. The colour is intense brownish gray

3 men) with RIEHL's melanosis since 1945 The disorder is seen almost solely in women. He blames photosensitization on a nutritional and probable endocrine basis

PIGMENTARY DRUG ERUPTIONS

Melanosis follows prolonged administration of *arsenic* or accidental chronic arsenical poisoning The drug is usually ingested in the form of FOWLER's solution. The skin becomes brown or grayish brown with multiple lighter perifollicular islands throughout (Fig 185), resembling a water splattered dusty surface SIMONS called this form leukomelanoderma punctatum or "taches négatives" Arsenical keratoses of the palms and soles usually accompany the melanosis. There is no satisfactory treatment, but vitamin A can be tried for its antikeratotic effect.

Many inflammatory drug eruptions are followed by post inflammatory melanosis. *Fixed eruptions* are especially apt to pursue this

course. They are at first urticarial in a local area, then the involved site becomes hyperpigmented with a grayish brown hue. Fixed eruptions recur in the same identical sites, with or without extension to involve other areas. They may be caused by ingestion of *phenolphthalein quinine quinidine bismuth coal tar derivatives* (acetanilid, amidopyrine, antipyrine, phenacetin, salicylates) and others Generalized medicamentous dermatitis including exfoliative dermatitis from *arsenic atabrine sulfonamides* and other drugs may be followed by generalized melanosis or leukomelanoderma (Fig 185)



185 Arsenical melanosis. The lighter perifollicular islands are characteristic

Argyria and *chrysiasis* follow prolonged administration of silver or gold medicaments. Localized argyria usually follows application of colloidal silver (argyrol or protargol) to the conjunctival sac, and imparts a brown colour to this mucous membrane. Systemic argyria is characterized by a grayish hue involving the entire cutaneous surface Treatment is unsatisfactory but suntan improves the appearance of the patient.

Atabrin, trypaflavine and other acridine derivatives make the entire body yellow. *Carotinaemia* is the designation applied to exaggeration of the normal yellow colour of the skin by ingestion of large amounts of carotene in the form of orange juice or rind, carrots pumpkins,

squash and green vegetables. The yellow colour is best seen on the palms and soles. Verification of the diagnosis can be made by chemical estimation of carotene in the blood serum. Decrease in the amount of carotene-containing foods is followed by reduction in the yellow colour

MELANOSIS IN INTERNAL MEDICINE

Melanosis is seen in several internal medical disorders. The best known is *Addison's disease* which is characterized by generalized brownish hyperpigmentation. The darkening is most pronounced at the sites which are normally hyperpigmented, namely—the nipples and areolae, axillae and genito-anal regions, and at sites of friction. The hair is darkened and has a brownish sheen. Generalized hyperpigmentation is also seen in some patients with *hyperthyroidism* occasionally in *malaria*, *Hodgkin's disease* and related disorders *abdominal tuberculosis* and *haemochromatosis*

Haemochromatosis starts as pigment cirrhosis which GILLMAN and GILLMAN found in a large percentage of patients with *pellagra* in South Africa. Cytosiderin is released by degenerating liver cells and may be taken up by the pancreas producing bronze diabetes, by the adrenal gland, producing addisonian hyperpigmentation, or by the skin, where it is deposited first about the sweat gland acini, producing a metallic gray hue, visible only in persons who are not too deeply pigmented. Haemochromatosis has been seen occasionally in persons who have received transfusions over a long period. Treatment of haemochromatosis depends on the presenting complication. Cirrhosis is universally present. *Bronze diabetes* is resistant to treatment and is only partially controlled by diabetic management, including administration of insulin. (See also chloasma page 179)

TREATMENT OF MELANOSIS

The cause should be removed, if possible. The patient should avoid exposure to natural or artificial ultraviolet irradiation in order to eliminate its stimulating effect. This procedure is especially important in persons with photosensitization melanosis. Addison's disease is fairly well controlled by medical management.

Local treatment of melanosis consists of application of substances to

produce mild desquamation. Many "bleaching" creams contain ammoniated mercury in five to ten per cent. strength. Any of the sulfur preparations recommended for treatment of acne vulgaris will produce sufficient mild exfoliation to be advantageous. A real "bleach" that operates by prevention of enzymatic action is "Agente Alba" an antioxidant used in the manufacture of rubber which is chemically mono-benzyl ether of hydrochinone. It can be applied in an ointment of 10 to 20 per cent. strength. It is necessary for prolonged intimate application for several weeks to obtain a result. Irregular contact with the skin will cause patchy depigmentation.

The only internal treatment which has been recommended for melanosis is vitamin C, which is given orally in high doses over a long period of time. Conflicting reports have been presented as to its efficacy

PIGMENTED NAEVI

Most reports indicate that members of the dark races do not have as many pigmented naevi as do Caucasians but HEWER stated that 95 per cent. of 200 Sudanese taken at random, of light brown to coal black colour, had easily detectable naevi. SAMBERGER stated that Negroes do not have hairy naevi *Dermatosis papulosa nigra* is a benign epidermal neoplasm and not a pigmented naevus.

EPHELIDES

Commonly known as freckles, ephilides are oval, round or irregularly shaped yellowish brown or brown melanotic macules varying from punctate lesions to those a few millimeters in diameter SIEMENS stated that the depth of pigment varies inversely as their size They are located on exposed surfaces, the face (nose, forehead, temples cheeks upper lip and chin) and neck which are exposed to a certain amount of ultraviolet radiant energy from the sun Other involved areas are the hands, arms and upper part of the trunk, especially the back in persons who sunbathe They are more frequent in light complexioned, especially auburn and sandy haired persons JANKOWSKY stated that red hair and freckles are seen together because of mosaic inheritance in the population of areas where races with a fair and a dark complexion intermingle PROSSER stated that freckling

seems to be due to a single dominant gene which is linked with that for red hair. Since the amount of sunshine is greater in the tropics susceptible individuals are prone to develop freckles there more than in other zones.

Ephelides appear in childhood, depending on the amount of ultraviolet irradiation to which the skin is exposed. SIEMENS stated that one-fourth of the total number of freckles is present at three years of age, one-third at four years, and one-half at five years. MATARASSO stated that the number remains constant after 25 years of age. They have their onset and/or become more prominent in summer and may or may not disappear in winter although they can always be seen in winter under ultraviolet irradiation. In very light complexioned persons the only cutaneous pigment may be in the epidermis of the involved areas, while in slightly darker persons, there is lighter diffuse pigmentation between them.

Freckles seem to be due to irregular distribution of enzymatic activity. The darkening of freckles in summer has been shown by FELSHER *et al.* to be the result of direct melanosis by long wave ultraviolet radiant energy (between 300 and 460 mm). Freckles are also darkened by roentgen and similar rays and BRUNNER *et al.* have shown that they are darkened by systemic administration of ACTH cortisone and pregnenolone.

Treatment of freckles is not entirely satisfactory and is carried out by mildly exfoliative preparations of which ten per cent. ammoniated mercury ointment is an example. MATARASSO recommended solid carbon dioxide applied long enough to cause a depression that persists for two to three seconds. Brief application of phenol, neutralized immediately by alcohol, has also been recommended. Protection from the long wave ultraviolet irradiation by an ointment such as one containing titanium dioxide is also of service. A newer treatment, namely a cream containing monobenzyl ether of hydroquinone, which may be used in strength of two to five per cent., is recommended by SCHWARTZ and PECK.

MONGOLIAN SPOT

Sacral spots are bluish macules varying from a few millimeters to several centimeters in diameter present on the sacral and adjacent

regions of the back. The ventral surface is rarely involved. They are present at birth and gradually fade out by the twelfth year of life. They have been called "Mongolian spots" because they were thought to be present only in Mongolians. They are seen in a varying percentage of deeply pigmented infants. (Fig. 186) They are rare in Caucasians although microscopic examination indicates that melanoblasts are present in the sacral region of most new-born infants, regardless of race. ASHMEAD considers the presence of Mongolian spot to denote admixture of negro blood an opinion not shared by others.

CHEMIN found sacral spots in 89 per cent. of Chinese children be-



186. Mongolian spots on Negro infant.
(Thatcher in Becker and Obermayer: Modern Dermatology and Syphilology)

fore the age of one year, 71 per cent. in those from one to three years of age and 19 per cent. from three to eight years of age. EL BAHRAWY stated that 90 to 100 per cent. of Mongolians, 100 per cent. of Malayans, 85 per cent. of Bolivian Indians, 65 per cent. of Negroes in Brazil, 52 per cent. of mixed races in Brazil, two to five per cent. of Italians in Brazil, 1.5 per cent. of Whites in Brazil and one per cent. of Whites in Paris have Mongolian spots during early infancy.

BRENNEMANN found sacral spots in 35 of 40 Negro children in Chicago. He believes that they occur in 95 per cent. of coloured children before they reach the second year.

MATUS found Mongolian spots in 75 per cent. (35 of 50 male and

40 of 50 female Negro infants) in South Africa. Extra sacral spots were present in 22 of the female and 17 of the male babies. GUTIERREZ and HIZON found Mongolian spots in 84 1 per cent. of 346 nurselings and small children in the Philippines. They quoted FINK as having found 94 7 per cent. in Burma. MACFARLANE found sacral spot in 38 of 50 newborn infants in Bengal. It is more common in the Himalayan region. In Jakarta Java, sacral spots were found in all of 15 native infants They were absent in Dutch infants and in Dutch-Indonesian hybrids.

Microscopic examination of sacral spot reveals the presence of fusiform melanoblasts between the collagen fibers of the superficial dermis

No treatment is necessary for typical Mongolian spot, since it gradually fades out. Melanoma does not originate in Mongolian spot.

BLUE NAEVUS

Closely allied to Mongolian spots are small, darker bluish macules which may appear at any time during life, and persist, or even enlarge steadily Microscopic examination reveals fusiform melanoblasts more densely packed than those in Mongolian spot.

LOEWENTHAL said that blue naevus or Mongolian spot had not been reported in adult Negroes. He did observe hemimelanosis facial and melanosis sclerae in a Negro about 25 years of age The melanosis had been present since birth and became less conspicuous as he grew older Microscopically the picture was that of a blue naevus. Similar plaques have been reported by others. They have been variously called *naevus fusco-caeruleus* *blue naevus* *progressive melanosis* and *persistent aberrant Mongolian spots* Conjunctival melanosis is sometimes an accompaniment. *There is no convincing evidence that melanoma arises in a blue naevus*

MELANOMA

While melanoma may not be seen quite as frequently in the tropics as in other zones it does not arise as frequently from a pigmented naevus and occurs predominantly on the heel and sole. STEVENSON reported 15 cases from India, many with definite history of trauma. Eleven were pigmented and four were non-pigmented.

Dr [illegible] found 17 melanomas in 18 malignant tumors in Northern Transvaal He stated that the degree of malignancy is lower

than in Europeans Smith and Elmes had 40 melanomas in 500 tumor specimens during eight years from natives of Lagos, Nigeria. Thirty of the 40 originated on the foot, suggesting trauma as causative. The average age of the patients was between 35 and 45 years.

Sequira and Vint found 67 melanomas in 539 malignant tumors from natives of Kenya. Thirty nine were from the foot and Hewer stated that, of 47 melanomas seen in 2500 specimens from natives of the Anglo-Egyptian Sudan at the Wellcome Tropical Research Laboratory 35 were from the lower extremity and 17 were from the sole. *In five cases, metastases were found in femoral or inguinal lymph nodes* with no sign of primary tumor Melanoma was as frequent in coal black Negroes as in lighter skinned Arabs

FUNGUS INFECTION

According to Castellani and Chalmers, certain *chromogenic fungi* Aspergillus, Microsporon, Trichophyton and others produce pigmentation of the involved skin. According to the colour the disorder is called *tinea alba tinea flava* and *tinea nigra*' Tinea nigra, caused by Cladosporium mansoni produces a black dull, lustreless colour The involved areas are usually the neck and upper chest. One European developed lesions on the palm. Neves and Costa recently discussed tinea nigra, and stated that it is confined to the East and the American continent In the western hemisphere it usually occurs on the palms as a black or brownish plaque which has resulted from coalescence of smaller macules The western variety is caused by Cladosporium wer neckii Treatment is by fungistatic and fungicidal remedies.

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CHAPTER 4

DEPIGMENTATION (ACHROMIA)

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A. MARCHIONINI Munich

Reduction, or absence of pigmentation of the skin may occur either *primarily* or *secondarily*—*i.e.* following other skin diseases of the affected part or parts.

A. *Primary depigmentation* may either be congenital or start during life.

1. *Congenital depigmentation* may be either total[1] or partial. If hereditary it is called *albinism* (albinismus universalis and albinismus circumscriptus).

2. If it occurs—like a birthmark—unilaterally it should be referred to as *naevus depigmentosus* to avoid confusion with albinismus circumscriptus. For these naevi (as is the case with all naevi, for that matter) are never familial: they are, in contrast to albinism, non-hereditary.

3. When primary depigmentation sets in later in life it is called *vitiligo*[2]. Vitiligo is a disease on its own: there are no other known typical forms of acquired primary loss of pigmentation. Most probably the Japanese and Pacific "*Safu*" should be regarded as a form of vitiligo (vitiligo reticularis of the legs).

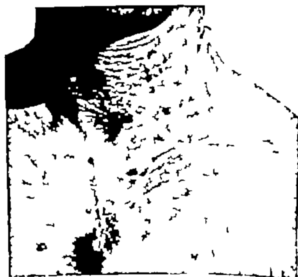
We gratefully acknowledge the cooperation of Dr. M. [illegible] *Munich* and Dr. F. [illegible] *[illegible]*.

[1] It is common knowledge that the Negro's skin at birth is often much lighter in colour than later. Complete pigmentation is attained within a few weeks ([illegible]).

[2] Vitiligo is a term used by Celsus for leprosy and morphoea. Bateman wrote that the "white and glistening appearance bearing some resemblance to the flesh of calves (vituli) seems to have given rise to the generic term vitiligo". Dunglison's Medical Dictionary states that it is derived from the Latin vitium for a blemish.

B On the other hand there exist a very large number of known *secondary depigmentations* which may result from every possible kind of dermal lesion or disease. For practical purposes these affections are referred to as *leukoderma*

I. Albinism, *i.e.* congenital, hereditary absence of pigment, is clinically and aetiologically a polymorphous syndrome. For practical purposes it may be divided, on the one hand as to its spread, into



187 Albinismus universalis in the Negro with pigmented lentigines. *(Pirrs Nairobi)*

"*total*" and "*partial*" albinism, and on the other hand as to its intensity into *complete* or *incomplete* albinism (Siemens).

a. In *albinismus universalis completus* pigment is absent from the entire skin hair and eyes The skin is accordingly crimson red (due to the blood vessels) the hair white and the eyes red. Close examination however invariably shows up small remains of pigment even in cases of "complete" albinism, especially in the eyes and in adults. In the white races no freckles will, as a rule, form on the skin but they are found in large numbers in the dark races (Pirrs). Lentigines too are

generally entirely without pigment in whites, so that they appear as bright red papillomata, whereas in dark races, they often contain much pigment (see Fig. 358). The eyes which at first are generally red, usually become a bright blue later on, and, in coloured races, may even take on a yellowish colour with tiny dark spots (PIERS). The hair of the head which is often silky, glossy and thin, takes on a reddish-

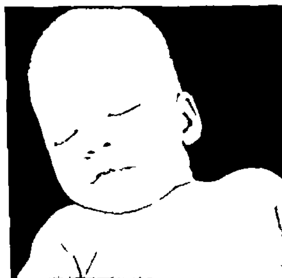


168. Albinismus universalis with cutis rhomboidea and pigmented lentigines.
(Piers, Nairobi)

yellow hue as soon as it grows longer; this, however, is not due to the formation of pigment but to that change in the horny substance to which SIEMENS has given the name of *Rotgelb Bleichung* (red-yellow bleaching), in contrast to the senile white bleaching. In such cases the ends of the hairs are accordingly most strongly decoloured.

Albinismus universalis is always coupled with other cutaneous

changes. Especially in places exposed to light, the skin often shows distinct *telangiectasias* as well as numerous fine wrinkles which, in the neck, develop into the well-known *cutis rhomboidea nuchae* picture. In addition one sees—apparently more often than in normal individuals—multiple *epitheliomas* and *senile keratoses* even already in youth so that one may be justified in classing albinism with the pre-cancerous



189 Albino or albinismus universalis in Ibo Negro child (Nigeria).
(Jelliffe–Ibadan)

dermatoses (PIRAS), in which respect it corresponds to "sailor's skin" (UNNA) and xeroderma pigmentosum (see Fig 382).

The most striking phenomenon is the simultaneous presence of *ocular disturbances* Not only are there photophobia and nystagmus—both caused by lack of pigment—but also, in nearly all patients, amblyopia in the majority astigmatism with either hyperopia or myopia, and frequently also strabismus.

That other skin eruptions (eczemas), susceptibility to all sorts of diseases, retarded or abnormal growth, disorders of the nervous system or defects of the intellect are especially frequent among albinos,

is quite unproven. Sun-erythemas, of course, do occur more readily but that goes without saying.

Universal albinism is a rare condition (1 to 10 000 of the cases of albinism). It is a recessively hereditary disease. It occurs in brothers and sisters with healthy parents. Parental consanguinity has been computed at at least 15 per cent. (WEINBERG). The disease has frequently been found "concordantly" in monozygotic twins.

In Negroes, universal albinism has been described relatively frequently, but this is probably because they show it more conspicuously. Primitive coloured peoples accordingly pay it their keenest attention. In some tribes, albinos are revered as higher beings; in others they are treated as outcasts and doomed to an unhappy, wretched life, when not killed after birth.

Synonyms: *achromia congenitalis, alphoderma, bedas* (Ceylon), *dondos* (Africa), *boakorro* (Guiana), *kakkerlak* (Java), etc. (see Fig. 189).

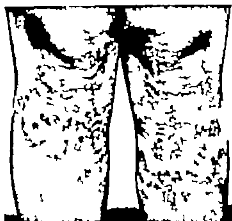
b. *Albinismus universalis incompletus* shows a great variety of forms. Complete albinos may get darker-skinned in later life, or it may be that the skin was not wholly unpigmented from the start. It is also possible for the skin to be entirely albinotic, while the iris is pigmented. If, conversely, the iris is albinotic and the skin pigmented, the case is not, of course, one of universal albinism, but merely one of ocular albinism.

Incomplete universal albinism has been given a variety of names, as *albinoidism, semi-albinism, leukism*. When found in Negroes it is also called *xanthism*. *Flavism* in animals also belongs to this group, and even, in a sense, also *rutilism*, since this is characteristically coupled with, admittedly, a freckled, but otherwise very poorly pigmented skin. There are, of course, any amount of *transitional forms* between this incomplete albinism and the normal fair hair and skin, although the latter may, after all, also be regarded as a moderate form of incomplete albinism. When incomplete albinism occurs in Negroes the skin is neither white nor pink; it shows a reddish bronze tint, sometimes with a yellowish hue. In these cases the hair, too, has a typical bronze-coloured gloss or a reddish hue (PIERS).

Susceptibility to certain diseases, such as eczemas, tuberculosis, and disorders of the eyes and nerves, is also supposed by some to accom-

pany not only incomplete albinism, but even fairness of hair and skin generally. This notion, however, is devoid of any reliable foundation in particular: for example, those ocular disorders which are so characteristic of complete albinism are no more frequent among incomplete albinos than among more strongly pigmented individuals.

Our knowledge concerning the hereditary factor in albinism is, as yet, quite inadequate. In some few cases the disease may, like the complete form, be of a recessive nature; in others it appears to be irregularly dominant. Remarkably enough, in the circumscribed form, localized



190. Albinismus areatus with hyperpigmented spots.

in the eye, albinism is recessively sex linked. Investigations are made very difficult because the diagnosis "albinismus universalis incompletus" comprises so many clinically and genetically different diseases.

Histologically total albinism shows a normal skin, in which the basal cell layer (stratum germinativum) and the cutis are unpigmented. In older albinos, moreover, we find on the uncovered parts of the body degenerative changes in the cutaneous tissue, especially in the elastica, which condition we know from "sailor's skin" and senile degeneration of the skin.

c. In *albinismus circumscriptus* pigmentation of the skin, the hair and the eyes is in general normal, but in several isolated places there are

large, irregularly shaped, white patches sharply delimited against the surrounding normally pigmented skin. Usually these patches are entirely unpigmented, particularly the borders (JADASSOHN); sometimes, however, we find albinotic areas which are not quite without pigment; in particular, there may be hyperpigmented spots inside the unpigmented white lesion and hyperpigmented indentations at its edge (see Fig. 190). The hair covering the white patch is also colourless.



191. Alb nmus circumscriptus in the Bantu-Negro (Tanganyika)
(Geigy-Basel)

These patches are stable, *i.e.* they do not change their form right through life; neither do they grow in size (apart from the fact that they become larger with the normal growth), although it does happen, especially on the covered parts of the body, that their real extent can be recognized only later, especially after exposure to the sun.

The patches have certain places of predilection, especially the middle

of the forehead just below the hair (*cf* the blaze in the horse) the middle of the extremities and of the abdomen, and are practically always multiple. For this reason the term "circumscriptus" may lead to misunderstanding and to confusion with naevus depigmentosus. Since the phenomenon occurs in a number of areas it might, therefore, be more apposite to speak of *albinismus areatus* The white areas are, in principle, always either symmetrical or median (which is merely a special instance of symmetry) but within certain limits—in common



192. Albinismus areatus or poliosis circumscripta.

with other symmetrical skin affections—they show some degree of irregularity within their symmetry (see Fig 191).

Since remarkably enough, the centre of the forehead just below the hair is a place of predilection, while the hair at this spot is also white (see Fig 192), a lock of white hair in the centre of the forehead is the most striking symptom of albinismus areatus especially in the black races Familial locks of white hair have been described as an affection on their own under the name of *poliosis circumscripta* (from polios = grey). We may assume, however that, also in these cases, other areas would have been revealed if the patients had been made to undress. In principle, of course there is nothing against the assumption that there may be abortive forms which are limited to the centre of the forehead or that they may be absent in the presence of other patches

of albinismus areatus up to the present, however, the occurrence of such cases has not been definitely proved. The term "*poliosis*" should therefore be avoided, as it prematurely assumes the existence of a separate syndrome, different from albinism.

Nothing is known of any correlation between albinismus areatus and other physical or psychic disorders

Albinismus areatus is a typically dominant hereditary affection of which many cases have already been followed up through many generations also in the so-called poliosis circumscripta form.



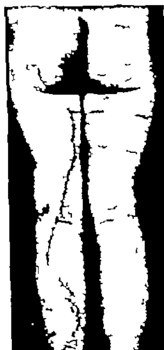
193 Unilateral naevus depigmentosus.

The unpigmented areas may naturally show differences in extent as between the several members of the same family these differences however keep within certain limits

There is an analogy between dominant albinism in man and the spotted or *piebald skin* of a great many domestic animals and which may also occur dominantly for instance in rabbits But in the first place the location of the colourless patches is in many cases not at all symmetrical neither are they inherited with the same localization and they constitute a still unsolved and enigmatic problem for the heredo-biological investigator Only a very small part of the phenomenon as found in animals therefore can be regarded as analogous with al

binismus areatus in man. To look upon the latter as being "spotted" therefore, is incorrect and must lead to misunderstanding

Albinismus areatus was first discovered in coloured people ("Elster and Leopard Negroes"). For this reason it was for a long time thought to be more frequent among the dark races. Once, however



194 Unilateral naevus depigmentosus with follicular keratosis.

attention had been called to it, it was found and described more frequently also in whites

II. **Naevus depigmentosus** should not be confused with albinismus areatus. The former, though admittedly also congenital, is—in common with other naevi—found "anywhere" without, that is, any favourite localization, and, moreover always or nearly always, unilateral (see Fig 193–194). It is indeed, truly "circumscribed" while neither the shape nor the size of the unpigmented patches undergo any

change throughout life. Familial occurrence of naevus depigmentosus is—also in common with other naevi—unknown. In monozygotic twins, it has often been found in one twin but not in the other and never so far concordant. Naevus depigmentosus is not, therefore, hereditary and as a matter of fact its precise cause is still a mystery It may be associated with a pigmentary naevus (see Fig 195)

Naevus depigmentosus may of course, also occur on the hair covered skin, for instance on the hair-covered head and make the hair



195 Naevus pigmentosus and depigmentosus.

participate in the trouble. In this case one sees a congenital lock of white hair which, however should not be confused with the dominantly hereditary poliosis in albinismus areatus from which it is distinguishable by the fact that it is not found in the latter's favourite locus but asymmetrically If the skin is not unpigmented at the base of the hairs—which, it appears also happens—then one has to do, not with naevus depigmentosus with leukotrichia, but with a "*naevus leucotrichoticus*"

The naevus depigmentosus should also be distinguished from an altogether different skin affection, *i.e* the *naevus anaemicus* which, as

regards form, localization, non-familial character and unilateral appearance closely resembles both naevus depigmentosus and any



196 Naevus anaemicus in one of a monozygotic twin.



197 Diascopic examination causing the border line of an naevus anaemicus to disappear

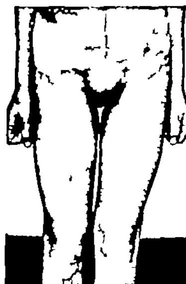
other genuine naevi (Fig 196). At first sight the naevus anaemicus looks exactly like a "white spot" (often, too a group of small white patches) such as the naevus depigmentosus. The difference however



198. Vitiligo: confluent spots.



199. Pinta-like vitiligo.



200. Bilateral, not fully symmetrical vitiligo.

is seen in diascopic examination at the edge of the patch, when the border line of the anaemic patch will, of course, disappear, whereas it will remain unchanged if the colour difference between the patch and the surrounding skin is caused by the difference in pigmentation (Fig. 197).

III. Vitiligo It is also possible for primary depigmentation to appear later in life, when it is called vitiligo This is characterized by the sudden appearance—without any other previous dermal changes such as erythema, etc.—of white patches in different places. These light-coloured patches grow peripherally are often, therefore, polycyclic, overlap each other and may eventually become so generalized as to leave only a few pigmented areas, or only a few small bits of pigmented or hyperpigmented skin (Fig 198). It is possible in such cases to mistake the diseased skin for the normal, and the remaining

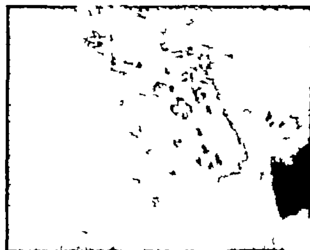


201 Vitiligo one of the predilection places. Note hollow edges of the borders.

pigmented parts for hyperpigmentations thus confusing vitiligo with chloasma (Fig 202), ephelides pinta (Fig 199), etc. What puts one on the right track in many cases is the fact that the alleged pigmented patches have hollow edges (Fig 201) Vitiligo generally occurs symmetrically although, here again, irregularities are sometimes found (Fig 200). Especially in the initial stages when the light patches are only few in number and when the patient's history is not clear this may make them appear to be unilateral, *with the* result that the disease is confused with naevus depigmentosus. We may of course also assume that vitiligo in common with all other



202. Vitiligo which can easily be confused with chloasma. In this case the hairs and lips are not affected.



203. Vitiligo with pseudo-follicular pigmented spots.

bilateral-symmetrical skin diseases may in exceptional cases actually occur unilaterally In such a case the distinction between vitiligo and a naevus depigmentosus tardus would be possible (if at all) only on the basis of the gradual growth and predilection of the patches

Vitiligo patches are, for the major part, completely unpigmented like those of albinismus areatus Often, however, the edge is hyper pigmented, especially where the skin is naturally already darker (on and around the genitalia, anus armpits neck) In generalized vitiligo moreover one usually has the impression that the re



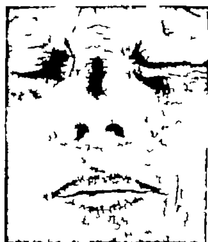
204 Two stages of discoloration in vitiligo ("Stufen vitiligo")

maining non-vitiliginous parts of the skin are hyperpigmented. We may conclude from this that, in vitiligo the pigment does not simply disappear but that there is a kind of "pigmentary migration" to neigh bouring regions Since such a migration can hardly be accepted, the effect of the depigmentation of the one part seems to increase the formation of pigment in the adjoining normal skin.

There often remains, within the area of the vitiligo a number of tiny pigmented spots about the size of a pinhead and mutually equidistant, for which reason they are generally held to be follicular pigmentary remains (Fig 203) Neither is the entire vitiligo patch necessarily com

pletely unpigmented it may merely be of a lighter colour than the surrounding skin. There may be completely unpigmented patches side by side with patches merely poor in pigment so that vitiligo may exist, so to speak, in two stages" (Fig 204) The decoloration of part of a patch may be so slight as to be unobservable in ordinary light and visible only in Wood's light (pre vitiligo MARCHIONINI) Especially in winter in the absence of the contrast with the *sunburnt normal* skin, such patches may appear to be cured In Wood's light however it will be seen that the cure was indeed, only apparent (MARCHIONINI).

Hairy skin may also be affected by vitiligo In these cases the hair



205 Vitiligo also affecting the red of the lips

may either remain incompletely pigmented, or it may join in the decoloration process Sometimes only a part of the hairs are affected, these giving the hirsute the appearance of being grey When the patches happen to appear near the centre of the forehead confusion with albinism is of course, readily possible at first sight but the patient's history and the finding of other patches not so atypically localized, will soon set this right Eyelashes and eyebrows (Fig 205) as well as the red of the lips (Fig 205) may also be affected by vitiligo

Although vitiligo does not show such restricted choice of particular

loci as albinismus areatus, it does show a preference for certain parts of the body In the first place, the part around the anus is nearly always affected (Fig 206), and this may accordingly decide the diagnosis in doubtful cases (Sternberg) Further, the genitals and surrounding part, the hands and fingertips, the coccygeal area and the neck are often affected. Then entire trunk, the extremities and the face are also commonly affected. A point of practical importance is that vitiligo may affect not only the anal region but also the parts around other openings of the body When this happens—as it not infrequently



206. Vitiligo predilection for the anus.

does—around the mouth and the eyes, it gives the face a clown-like look (Fig 202) which makes the patient conspicuous wherever he goes, so that he may feel forced to cease appearing in public altogether

This localization around the openings of the body (including the nipples) has, however another far more general significance, which is subject to some enigmatic law Vitiligo is also localized with a certain preference on and around every possible kind of skin affection, chiefly in the form of a white "background" That it is found on pressure spots (Fig 207) and in scars may be explained if one

assumes the existence of a locus minoris resistentiae. On the other hand, a most remarkable thing is the localization of vitiligo around both pigmented and unpigmented lentigines (Fig 208) This phenomenon, which has been recognized by HEBRA (even, it seems to the painter of the Isenheim altar MATTHIAS GRÜNEWALD) was later held by SUTTON evidently wrongly to be a syndrome on its own (SUTTON s *disease or leukoderma acquisitum centrifugum)* whereas it is merely a simple *vitiligo perilentiginosa* with which larger genuine naevi may also be affected (vitiligo perinaevica,, in common with every possible other skin disease, as tuberculosis verrucosa and lupus ery



20 Vitiligo predilection for pressure spots (garters).

thematosus The cause of this conspicuous choice of localization on the part of *consecutive vitiligo* is still a mystery

But the development of vitiligo too, is just as enigmatic. Its first appearance takes the patient by surprise, and the subsequent course the eruption may take is just as incalculable. It may cease completely at any moment it may extend slowly and gradually or it may stop and then start again after a long pause Slow growth and ultimate cessation is most frequent Spontaneous regression may be possible in any case that would be extremely rare On the other hand, pigmented spots have been seen around the edges of vitiligo patches, in places which previously had been unpigmented (SIEMENS) The appearance of similar small pigmented spots has also been observed within the vitiligo patch after therapeutic experiments especially after irradiation There

is, however no practical advantage whatsoever in this, because these newly pigmented spots only make the vitiligo more conspicuous and ugly than it already is.

The unpigmented skin in vitiligo is hypersensitive to the sun's rays owing to the absence of pigment and its protection against light. As a result photo-erythema may readily appear on the white patches We do not believe that there is such a thing as an initial erythematous stage. Perhaps pruritus may precede vitiligo To chemical and toxic stimuli the depigmented parts appear to be less sensitive the hyperpigmented



208. Leukoderma acquisitum centrifugum or vitiligo perilentigosa.

border zone, on the other hand, hypersensitive. It is possible that this is only due to differences in the accustoming to light. In many cases it has been stated, there is reduced secretion from the sebaceous and sweat glands in the affected parts. In the tropics one should beware of the "vitiligo being leprosy in such cases. There is no increased urticarial dermographia in the white areas, but "red dermographism" it appears, may be caused more quickly and distinctly This may be merely because the red marks are more clearly visible on the white skin.

The capillaries are (allegedly) contracted but this cannot be an important factor since no differences in temperature could be determined as between the decolourised and the normal skin. Neither can we assume any direct causal relation with the nervous system. It is clear that the disturbance is cellular in character, since exchange transplantation of pieces of skin failed to produce either pigmentation of the decolorized, or decoloration of the pigmented skin. A most remarkable thing is that the vitiligo not only has a tendency towards localization around cutaneous lesions, but that, conversely it is also—if less often—seen that the lesions of other skin eruptions have a marked tendency to appear either in the centre or round the edges of long-existing vitiligo

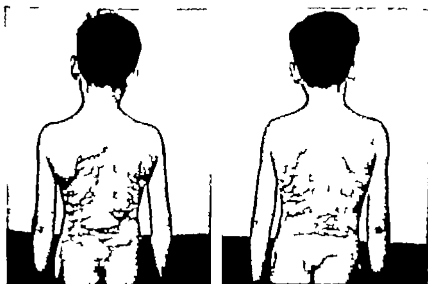


209 Vitiligo has not only tendency towards localization around cutaneous lesions, but it is also seen sometimes that skin lesions have a tendency to appear in the centre of vitiliginous skin.

(Fig 209) In other cases (*e g* eczema) the vitiligo may remain unaffected Looked at from the angle of certain dermatoses therefore the vitiliginous skin would appear to be changed also functionally in some way or other TOURAINE considers vitiligo to be a form of radiculitis posterior on account of the so frequently segmental or radicular spread. In common with ROBERT the present writers doubt the correctness of this view

In a few cases the impression was that vitiligo occurs more frequently as a concomitant of internal disease especially in BASEDOW'S disease and tabes dorsalis. One of us (SIEMENS) saw a most pronounced

instance of this in a case of ADDISON's disease. We cannot yet decide, however whether such cases are not pure coincidence vitiligo, after all, is far from being a rare disease. The most probable interconnection, in our view is that between *vitiligo and alopecia areata* this having been described fairly often. In this, of course, the unpigmented hair appearing in alopecia areata during the stadium reparationis, and



210 and 211 Concordant case of vitiligo in monozygotic twins.

which, in older people, remain colourless, should not be confused with vitiligo of the hair-covered head.

The cause of vitiligo is unknown. It is true that the literature contains, maybe, a dozen reports of familial cases and one of the writers (SIEMENS) once saw a case of two adult brothers with vitiligo showing a closely similar spread. But in a relatively so frequent disease these are surely very meagre findings, which argue rather against, than in support of a hereditary factor For this reason it is indeed, most remarkable that both sets of twins with vitiligo that have, so far been described (HANHART SIEMENS) were found to be concordant cases not only as regards the presence of the patches but also as regards their type and spread (Fig 210 and 211) Here, therefore, we find a certain

contradiction as between the observations in families and those in twins. Clarification must be left to the future.

Vitiligo in coloured people has often been described but in their case the chance of confusion is greater on account of certain tropical leukodermas which may resemble vitiligo. Again it has been suggested that vitiligo is less frequent in Indonesia, both among natives and among Europeans (POLAK). The contention that, in Europe,



212. Leukopathia symmetrica progressiva reticularis (Matsumoto). *(Obs. G. Costa-Belo Horizonte)*

it is especially frequent among brunettes seems to us doubtful, if only because they would show it sooner. No systematic investigations into this question have been made up to now. Primitive peoples sometimes treat vitiligo patients as outcasts, probably because they confuse vitiligo with macular leprosy. (See also the Old Testament.)

Histologically vitiligo shows, in accordance with the clinical picture

lack of pigment in the actual patch, and an excess of it in any hyper pigmented adjoining parts that may be present. In addition, however the unpigmented area may contain "MASSON's cells" which, under the influence of certain stimuli may change into melanoblasts (MARCHIONINI). ROBERT found reduction of the iron content of the serum, and an increased aneurin thiamine content in a dermal dialysate.

A primary and progressive achromia is also the *leucopathia punctata et reticularis symmetrica* which has been described in Japan and some



213 Analgesic leukoderma in tuberculoid leprosy
(Simons Amsterdam)

Pacific islands by MATSUNAGA and MATSUMOTO. It is also called *Safu*. This form is confined to the legs and in some cases is hereditary From a clinical point of view we regard this type as a subtype of vitiligo (Fig 212)

IV Leukoderma. For practical purposes the collective term for all secondary depigmentations is leukoderma. It constitutes the counter part to secondary hyperpigmentation (melanoderma, SIEMENS), and

owes its existence, in principle to the same causes *Every cutaneous lesion from simple pressure and friction to scratches and deeper wounds every inflammation or other deeper morbid process in the skin may lead to disturbance in the production of pigment either in the form of hypo- or hyper pigmentation* In the case of scarring processes, either leukodermic or—less often—leuko-melanodermic scars may form. If there are no structural changes in the skin, then either leuko- or melano-derma is formed *i.e.* in a sense as *cicatricial equivalent*" (SIEMENS). Quite well known are those

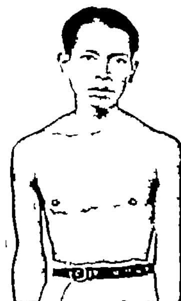


214 [illegible] leukoderma in seborrhoic eczema of the cheeks and nose which was initially regarded macules of tuberculoid leprosy (see also Fig 24)

(Simon Amsterdam)

leukodermas which remain after syphilitic roseoles (*leucoderma syphiliticum* or *collier blanc de Vénus*") and leuko-melanoderma in *leprosy* when they are coupled with anaesthesia. Both leukoderma and melanoderma are also very frequently seen in psoriasis (leukoderma psoriaticum) they may however follow any other not too acute inflammation of the skin (See Fig 214) One form which is often seen, but not often described is that in yaws and called *leucoderme pianique*" (SIMONS) (Fig 19) This leukoderma, under the yaws crusts is differ

ent from what is called *pintoid yaws*" (see Fig 216) for the latter is either a combination of hyperkeratosis palmoplantaris, achromia and juxta articular nodes (GUIMARAES) if not of pinta and yaws, or yaws in a vitiligo patient (SIMONS) Especially leukoderma is found in super ficial fungous diseases (*achromia parasitaria*) Here, however it is not certain whether, or to what extent, it is the photo-protective action of the crusts or possibly the fungi or retardation in the production



215 Achromia parasitaria due to tinea fla a
(*Simons– Amsterdam*)

of pigment, caused by accelerated desquamation, or again, the direct damage to the pigment building cells due to the toxic action of the parasitical products, that is the cause of the depigmentation. That the latter factor plays a role may be concluded from the fact that, even after complete recovery from the fungous disease the patches may subsist for many years (ee Fig 215)

One disease which may specifically cause leukoderma is *pinta* (de

scribed separately in the present work) It is highly probable that, in such cases, the leukoderma appears subsequently to the active lesions. (see Fig 217)

A syndrome coupled with marked formation of white patches has



216 Leukoderma following yaws When diffuse it is called pintoid yaws
(Lars Caragen)

been described under the name of *tinea albigena* It may well be supposed, however that we have here to do with exceptionally severe cases of leukodermatous pinta or perhaps vitiligo only (SIMONS) (Fig 20) Owing to the conspicuous appearance on the dark skin, leukoderma

in the tropics may be confused with vitiligo, or even with albinism, a thing which would hardly happen in northern regions.

In common with vitiligo patches, those in leukoderma may be completely unpigmented. In the latter however—far oftener than in vitiligo—it is a reduction, rather than the complete absence, of melanin from the skin *i.e.* a mere hypopigmentation. In accordance with this the course of the affection is in general, more favourable. The less-pronounced leukoderma usually shows a spontaneous regression. It may however last for months and even years, as may be seen even



217 Pinta from Brazil.
(Orig. G. Castro-Belo Horizonte)

in leukoderma in scars. Strongly developed leukoderma, on the other hand—which admittedly is much rarer—may remain right through life.

Since leukodermas and melanodermas can be traced to the same causes, it is not surprising that they may also occur in combination, when they are called "leuko-melanoderma". In most cases of this kind one finds unpigmented spots or patches within a hyperpigmented area of the skin. They are most frequently found after treatment with arsenic and after insolation.

Light patches may also be caused by the administration of medicaments, especially chrysarobin in psoriasis they occur for preference around the foci and have nothing to do with the formation of pigment, but are conditioned by the colouration and differences in the desquamation of the horny layer They are called by many authors *pseudo-leukoderma*

The cause of the leukodermas is complex on the one hand they are conditioned by external factors (light friction, pressure [1]), on the other hand by the particular nature of the disease (syphilis, pinta, psoriasis dermatomycoses) and, finally to some extent, by the patient's individual disposition

Histologically leukoderma shows either a reduction or the complete disappearance of pigment from the epidermis while there may be some pigmentary remains in the cutis. Slight inflammatory or other morbid phenomena may of course, often be found in the connective tissue and vessels as the aftermath of the pathological processes which led to the decoloration.

Leukoderma as well as pigmentations may occur in old scars When punctate they may look like *white spot disease* this name however indicating punctate scleroderma.

There is one affection which has nothing whatsoever to do with depigmentation, although its (hitherto most customary) name might lead one to think so namely *incontinentia pigmenti* This condition, which sets in shortly after birth and is preceded by an inflammatory stage is characterized, not by depigmentation but by the appearance of small steel grey pigmented dots specks or asterisk-shaped patches owing to the removal of pigment from the epidermis to the cutis. As DOORNINK has ascertained, the insufficiency of the epidermis to retain its pigment may also be found in all sorts of other dermal abnormalities Incontinentia pigmenti therefore, is a general pathological concept and the term is not appropriate as denoting any specific syndrome. The authors accordingly propose to call this disease so long as

[1] A most interesting form is leukoderma due to hydroquinone-antioxidant (agerite alba) from rubber gloves FREEMAN and HARRN have described leukoderma of the lips in trumpeters This might be due to pressure as well as to a chemical action of the metal

our knowledge of its essential nature is still limited, after the authors who were the first to describe it, *i.e.* SIEMENS-BLOCH pigment dermatosis. This would also eliminate the possibility of its being confused with the depigmentations.

THERAPY

The therapy of the various forms of depigmentation leaves us little hope. In the case of leukoderma it is best to wait for a possible spontaneous recovery. Artificial sunlight irradiation of vitiligo after previous application of bergamot oil to the white patches has turned out a disappointment to the greatest expectations. In addition, all these irradiations entail the risk of causing spots (freckles) and hyperpigmentation of the parts around the white patches. Internal treatment by means of chemotherapeutic substances and hormones has frequently been advocated, but has been proved valueless by subsequent tests. Vain efforts have also been made to find a useful tattooing method. For these reasons there seems to be more likelihood of success in attempts to lighten the colour of the surrounding skin, in order to make the difference less conspicuous. This may be done—true, only in a few suitable cases—by means of bleaching substances for instance, 2 per cent. mercuric chloride in vaseline. In all other cases the least one can do is to warn the patient against unduly strong light, or prescribe a photo-protective lotion (cibazol spirit para-aminobenzoic acid PAB). Satisfactory results may sometimes be obtained by intracutaneous injections of autohaemotherapy causing the formation of new melanin corpuscles in the melanoblasts, and chromatophores. It has also been stated that intradermal injection of melanophorin hormone was successful in many cases, when accompanied by intramuscular injection of hormone containing melanin (200 units weekly). According to some reports in the literature, intradermally injected toxins have a pigment forming effect, which however may be explained by the accompanying inflammatory phenomena. Most important of all, however is to induce the patients, by appealing to their common sense, to help themselves by cosmetic means, as regards the most important places—such as the face—by applying an artificial stain, *e.g.*, potassium permanganate solution. Psychotherapy has only given accidental results, it is usually

a waste of time and of money. Because of the variable course of vitiligo and leukoderma it is always difficult to assess the effect of any therapy.

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DISEASES DUE TO PROTOZOA, SPIROCHAETES AND RELATED CONDITIONS

HISTORY AND EPIDEMIOLOGY

Early reports about venereal diseases in the tropics are scanty and they are inconclusive because many of them, as ZECHMEISTER pointed out, were written not by physicians but by missionaries seafarers traders or scientists (LEO AFRICANUS CHARDIN VOLNEY FORSTER, HORNEMANN) More authentic information became available during



218 Extragenital primary lesion in a Javanese.
(Van der Zyl – The Hague)

the nineteenth century when a larger number of physicians travelled in the tropics or were sent there by government or other agencies or practised there for prolonged periods and comprehensive surveys of the geographical distribution of syphilis have been compiled by JULIUS HIRSCH DAVIDSON GELAROW and others From the quotations of HIRSCH s book (1883) it is evident that, at that time syphilis was widespread in all tropical countries with the possible exception of a

few areas, the remote inner parts of Central and South Africa, for instance, and some Pacific islands. Incidentally the latter still seem to be relatively free of the disease up to the present time (Horack).

As interesting as Hirsch's statements may be, they have only limited value because the investigators whose reports he has quoted having no knowledge of bacteriology could make no sharp distinction between syphilis and other venereal



219 Giant extragenital chancre with secondary papular syphilid on the face.

diseases, such as chancroid and lymphogranuloma venereum. Hirsch, on the other hand, noted the differences between syphilis and yaws. As complete as possible coverage of the subject was given by Scheube (1902) who sent questionnaires to a great number of physicians who had observed venereal diseases in countries of warm climate. From the fifty-nine replies, he concluded that the distribution of syphilis in tropical and sub-tropical countries was almost universal. There is, moreover, a noteworthy similarity between his and Hirsch's statements regarding the few tropical areas in which syphilis was rare or absent. Similar observations were reported by Wurtz and Thiroux.

With the progress of colonization and deeper penetration into the tropics, the reports increased in number and reflected more thorough study although they still contained contradictions and showed variance. This was due to the fact that on the one hand reliable statistics were lacking, and on the other syphilis was often confused with yaws

In 1908 LAMBKIN found that 90 per cent of the population of Uganda was syphilitic, but LAMBKIN's statement was criticized immediately as a great exaggera-

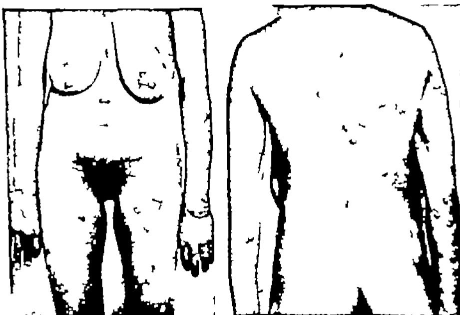


220 Submandibular adenopathy due to primary syphilis of the lower lip

tion by Cook who found that only 14 8 per cent of his patients had syphilis and estimated that no more than half of the population of the Protectorate was infected In 1912 KEANE also described his clinical observations of syphilis in that territory Much later DAVIES (1947) maintained that LAMBKIN and KEANE wrongly diagnosed yaws as syphilis. KÜLZ (1908) stated that he observed syphilis among 12 to 28 per cent of the native workers in a part of Cameroon where investigators who studied the situation ten years previously had not seen syphilis at all

[illegible] (1902) spoke of the wide diffusion of the disease over all Africa calling Port Said especially *"the paradise of syphilis"* STEUBER found syphilis widespread among the Negroes of East Africa, at that time a German colony ROTHSCHILD (1908) investigated syphilis on several trips to Central America,

where the people of Nicaragua and Panama particularly appeared to be affected. LACAPÈRE (1923) who devoted a lifetime to the study of syphilis in Tunis, Morocco and Algiers, reported a prevalence of 70 to 80 per cent among the Moslem population of these countries. NOGUE (1924) found syphilis widespread in Dakar and the whole territory of Senegal. CHARPENTIER reported from French Congo that one third of his hospital patients had syphilis. In 1926 STANNUS gave an "excellent critical review" (STRONG) of the literature on syphilis and yaws written during the period from 1914 to 1925 In spite of the insufficient statistics and the inaccura-



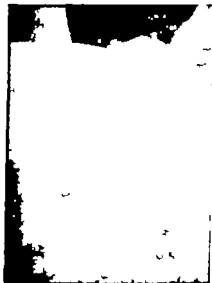
221 222. Generalized papular syphilid in early syphilis.
(New York Skin & Cancer Unit Dr M B Sulzberger)

cies in diagnosis which STANNUS stressed "the wide distribution of syphilis among the natives to some extent may be recognized" According to CASONI (1915) 100 per cent of the Arab population of Libya was affected with syphilis. HERMANS (1927) rarely saw early syphilis among the natives in some districts of Java, but reported, quoting SMITS, that whole transports of coolies had to be hospitalized because of venereal diseases and that in one transport 16 per cent of the women had florid syphilis. BERCOVITZ (1924), solely on clinical observations considered 50 to 60 per cent of the population of Hainan to be infected with syphilis, and MAXWELL (1927) estimated that 15 per cent of the general population of China had the disease JEANSELME wrote in 1931 that "among the natives of Africa, Asia and the Far East syphilis forms enormous foci."

It seems that conditions have not changed greatly during the last twenty years. GUTHE and REYNOLDS made a statement in 1951 that in Europe, North America, Australia, and limited areas elsewhere, effective treatment of millions of affected persons has contributed to an accelerated decline in the incidence of syphilis but that this is not the case in the underdeveloped areas of the Middle East, Africa, the Pacific areas, and South America which are inhabited by more than



223 A noliform secondary syphilid
(Fasal – San Francisco)



224 Varicelliform secondary syphilid
(Van der Zyl – The Hague)

two thirds of the world's total population, and in which the great infective reservoirs of syphilis are found. This opinion is supported by many reports from those areas. According to HOWARD (1942) syphilis was common among natives of the Sudan, of whom it was estimated approximately 40 per cent had some type of venereal disease. TOBIAS (1944) estimated that about 15 per cent of the native inhabitants of the Transkai part of the Cape Province of South Africa, were suffering from syphilis. In 1945 STRONG wrote that "syphilis is rampant in large parts of the tropics". The report of

WILLCOX (1946) from West Africa stated that syphilis in the four colonies (Nigeria, Gold Coast, Sierra Leone, and Gambia) was more common than is generally supposed and much more so in Northern



225 Hypertrophic lesions around the nostrils in early syphilis.



226. Condylomata lata.

Nigeria " In discussing WILLCOX s report, MCELLIGOTT mentioned that "there were enormous reservoirs in the Far East—Singapore, Hongkong and Rangoon and stated in 1949 that "syphilis is

extremely common throughout the length and breadth of detribalized tropical Africa and it is now rapidly penetrating the tribal areas."

PREBBLE reported in 1946 from India that no accurate estimates of the incidence of venereal diseases were available but that it hardly could be doubted that it was



227 P[illegible] cle papular lesions with central hyperpigmentation showing predilection for the orifices "the most striking dermatological peculiarity in the Negro"

[illegible]ery high. The same opinion was offered by R[illegible] in 1947. According to [illegible] (1946) there was a high rate of incidence of syphilis and gonorrhea among the natives of South Africa; he wrote: "Some tribes are affected so heavily that they are in danger of extinction." Dr [illegible] (1948) considered the rate of incidence of syphilis among Africans in Kenya about 25 per cent. He observed the continuous increase of the disease and mentioned that from January until June 1940 of 645 African domestic servants examined in Nairobi 230 were found suffering from



228. Papular squamous (psoriasiform) lesions of polycyclic arrangement.



229. Circin[illegible] papular lesions with central hyperpigmentation.

syphilis. KARK (1949) said "that few countries can have a higher incidence of syphilis than South Africa" the results of serological examinations of the natives revealed that more than 40 per cent. were positive in some groups. McKAY (1950) found that in Masai, a province of Kenya, "syphilis increased alarmingly during the last twenty years from a trivial incidence to the position where at least one in every five persons became infected" CUTLER found in 1949 a very high incidence of syphilis among the people of Afghanistan, although some patients seemed to present one of the endemic varieties. The same author made serological tests in one district of India, where he found 70 per cent of the adult population suffering from syphilis.



230 Keloid formation as residue of ulcerated nodules.

The best over all picture of the situation can be obtained from a paper published in 1948 by GUTHE and H[illegible] who compiled figures illustrating the prevalence of syphilis in many countries of all continents. Although the statistics used were based on different principles, they clearly indicate the much higher incidence of the disease in those countries which are inhabited predominantly by coloured races.

In the United States the fact that syphilis is more prevalent in the coloured than in the white population is generally recognized (M[illegible], V[illegible], P[illegible]

HAZEN, VONDERLEHR and USILTON and many others) while SMILLIE went so far to call "syphilis in the United States primarily a Negro problem." As an adequate summary of the situation, the following quotation from a recent paper by DEOLER is sufficient "Of the 20 489 cases of syphilis reported for the first time in New York City in 1949 6 749 were said to have occurred in the white population, 11,951 among Negroes, and 1 128 among other non-whites, mostly Chinese and Japanese adult males. In 661 cases the race was not stated These figures would indicate a syphilis annual rate of 94 per 100,000 in the white population and of 1,923 in the combined non-white population, when the average rate for the entire city was 261 Somewhat similar information is available for the United States as a whole for the fiscal year of 1948, when the registration rate in the white population was 99 per 100 000 and 1,376 in the non-white population, with an average rate for the whole country that year of 235."

SYMPTOMATOLOGY

MOORE has said that "syphilis tends to follow certain definite disease patterns in different racial stocks" Notwithstanding the difference of opinion on the explanation of it, which will be discussed briefly later, this fact is generally accepted (STOKES, CHESNEY BUSCHKE and JOSEPH LEWIS, DATTNER, KAMPMEIER, FRAZIER and HUNG-CHIANG). The peculiarities of the disease observed in the darker races and its contrast with European syphilis caused the French authors to coin the term *exotic syphilis*" (JEANSELME, WURTZ and THIROUX, GAIDE, LACAPÈRE, SÉZARY) a term which was meant to refer not to a different aetiological agent but to its distinctive clinical course and manifestations.

A. NON-DERMATOLOGICAL MANIFESTATIONS

Before the characteristics of the skin lesions in coloured people are described, at least two other aspects of clinical and pathological differences must be discussed briefly

First, it has been stated repeatedly that cardiovascular syphilis occurs more frequently in the coloured races than in the white (ZIMMERMANN, TURNER, HAZEN). For instance GLASER found cardiovascular syphilis approximately four times more common in the black than in the white race. But reports about cardiovascular syphilis in African natives are ambiguous. DE MELLO stated that aortic aneurysm was rarely seen clinically and at autopsies. While GRIFFITH in Johannesburg found in 4,047 autopsies that the ratio of aortic syphilis between non-Europeans and Europeans was 12 to 1 BECKER, who examined 3 000 autopsies in another mortuary of the same city concluded that syphilis was not a cause of cardiovascular disease in the Bantu and coloured races in a large number of instances. MANSON-BAHR, however considered vascular heart disease in the tropics usually syphilitic and D TES found that aortic syphilis was by far the most frequent cause of sudden death in Africans

Of even greater interest is the incidence of neurosyphilis, in particular its parenchymatous type, in coloured races. Greatly divergent statements can by found in the tremendous number of studies that were published on this exceedingly controversial subject.[1]

Almost all of the reports of the nineteenth century and the majority of those



231 (reunat secondary lesions have als pred lketu n for the ge itals Case of a cutaneous "mono relapse" in a Chinese Ja
(Simon [illegible])

from the beginning of this century maintain that parenchymatous neurosyphilis was absent or very rare among the natives of tropical countries ([illegible])

[1] After this chapter was finished the following paper was published by R. R. Willcox: Some Observations on Neurosyphilis in the African Negro. *J. Ven. Dis. Inform.* 32: 229 (Sept.) 1951, which contains an excellent discussion of this topic.

as well as among the American Negro (ZIMMERMANN, TURNER, HASEN). For instance, ZIEMANN (1902) did not see any cases of paresis in the insane asylums of Trinidad, nor did he learn of the occurrence of any in Venezuela in spite of assiduous inquiries he saw tabes in Negroes in the tropics only in two cases, both of them in Jamaica. ROTHSCHUH (1908) reported that serious changes of the central nervous system caused by syphilis were not known in Central America. In Java, NIEUWENHUIS (1911) declared that "tabes and paresis did not occur at all" and HERMANS reported that syphilis of the central nervous system was "rarely or never

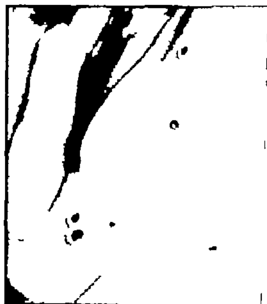


232. Circinate hyperpigmented lesion of the hand in late syphilis.

seen among untreated natives" According to HAUER, in the early nineteenth century "metaluetic diseases" were not observed at all among the coloured people in that part of East Africa, which then was [illegible] German colony. LACAPÈRE (1923) stressed the extreme rarity of both general paresis and tabes in North African Moslems. MACARTHUR (1923) ne[illegible] saw tabes or paresis among the Bechuanaland natives. BERCOVITZ (1924) reported that he had not seen any case of paresis among the extremely syphilitic population of Hainan [illegible] eight years of practice and only three cases with the diagnosis of early tabes.

Subsequent investigations, how[illegible] ha[illegible] brought out the fact that either

conditions have changed since the first decades of this century or previous reports were based on faulty diagnoses. This impression is supported by the critical review of MONTEL (1942). GELFAND (1948) also pointed out that neurosyphilis is by no means uncommon in the Africans, although the incidence of the meningovascular type is much higher than that of the parenchymatous pattern. As far as America is concerned, PLAUT (1925) proved in his monograph that general paresis existed prior to and at the time of his study among American Negroes, and that at least some cases were observed in Negroes in Cuba, as well as in American



233 Ecthyma syphiliticum of the upper arm.
(Van der Zyl – The Hague)

and Mexican Indians. More recent reports, moreover, showed high incidence of paresis in American Negroes, although DATTNER (1944) as a result of his experience in Bellevue Hospital in New York, considered the incidence of parenchymatous neurosyphilis "certainly much less frequent" among Negroes than among whites. Reporting from the Virginia State Hospitals KO[illegible] (1940) stated that the ratio was 15 to 2 between coloured and white paretics newly admitted to the hospitals. KIRSCHBAUM (1945) was led to the following conclusion by extensive clinical and post-mortem studies: "General paresis occurs, according to the syphilis rate, as frequently in the Negro as in the white population in this country" but he acknowledged the rare incidence of neurosyphilis among other Negro stock. In contrast to KIRSCHBAUM's statement, COOK (1948) maintained from his studies in Trinidad that "neurosyphilis is not a

rarity in the tropics. In conformity with this view are the findings of Murgatroyd and Trowell who on reviewing 269 cases treated in a mental hospital in Uganda from 1940 to 1942, found that neurosyphilis in all varieties was present in 13 cases, but that tabes was very uncommon. Hutton reported from the same country in 1949 that all forms of neurosyphilis except tabes dorsalis were common and might be expected to become more so. Leys (1947) stated "The African natives do suffer from cardiovascular and neurosyphilis but probably not in as large a proportion as do the European races." In contrast to these and similar reports, there are found in recent textbooks and periodicals statements such as "All tropical workers have noted the absence of tabes and paretic manifestations in the native syphilis" (Strong, 1945). "Syphilitic diseases of the central nervous system such as tabes and general paresis are seldom observed in Central Africa" (Manson-Bahr). "In spite of the high prevalence of syphilis in the natives of the tropical countries, the absence of parasyphilitic disease is very striking" (Hauptmann) and "the white race is known to be more susceptible to neurosyphilis than the Negro." (Weiss and Joseph). According to Van Wulfften Palthe the clinical picture of tabes dorsalis and progressive paralysis in coloured inhabitants of tropical countries differs from that usually seen in western countries. In Indonesia the central nervous system is more frequently affected than the autonomous-vegetative nervous system. Optic atrophy is often an initial symptom.

B. Dermatological Manifestations

1. Early syphilis

The primary lesion of early syphilis, chancre, is not essentially different in the various races. It has been reported that the chancre is infrequently seen in some tropical countries (McArthur and others), but this may be explained readily by the fact that the primary lesion is usually not painful and, therefore, does not cause primitive people to pay attention to its occurrence. Keith Fraser, writing about syphilis in South African natives, stated "whether the chancre is a rarity or not is not clear. The fact remains that in native areas it is very seldom seen" but "more frequently ... in town natives". Phagedenic ulcers which leave extensive disfiguring scars are not common in American Negroes. Mixed chancres, however, are extremely common in the tropics (Tarayre, Barkhuus, De Mello), and Keith Fraser reported that it "is rare to meet with uncomplicated chancres". The mixed infections are caused by pyogenic organisms or produced by Hemophilus ducreyi which may be almost the normal flora of the Africans (Young). In most cases they are complicated by massive bilateral involvement of the inguinal lymph nodes, followed by ulceration

in the groins. Multiple primary lesions have been observed (ATKINSON, DE MELLO) but not a number sufficient to have significance as a racial characteristic. The fact that extragenital chancres are a rarity in Negroes has been noted by all American syphilologists, but on the other hand, they are not uncommon in Asian and African natives (JEANSELME, LACAPÈRE). DE MELLO for example saw in the Africans on many



234 Serpiginous nodules in late syphilis.

occasions cases with a genital sore and several extragenital sores in the patient. REASONER offered the suggestion that extragenital chancres were rare in Negroes because their tissues with the single exception of the genitalia have a defence against initial syphilitic infection, a theory which was called "highly disputable" by HAZEN. *The secondary manifestations of early syphilis* in coloured patients differ from those in whites in several respects, particularly in the later

secondary stage of the disease. Very common in Negroes is general *adenopathy* with pronounced enlargement of the cervical, epitrochlear and axillary lymph nodes HAZEN however called attention to the fact that lymph nodes are normally more noticeable in coloured than in white people STOKES reported that he and his co-workers had not seen uncomplicated general adenitis of syphilis to reach the proportion of the marked adenitis of early HODGKIN's disease or lymphatic leukaemia" but that he learned from MOORE that this may occur in



235 Grouped and gyrate ulcers with partial scar formation in late syphilis.

Negroes Moreover in early syphilis "coloured patients have *eye involvement* more than three times as frequently as white patients" (STOKES).

Of the secondary manifestations "perhaps the most striking difference between coloured and white syphilitics is in the skin lesions" (LEWIS). The *macular rash* common in whites is rare in Negroes, but the shades of colour among tropical peoples present such a wide variation that mild changes can be distinguished only with difficulty (SCHEUBE, DE MELLO and many others), and particularly in the very dark skin a macular eruption may be "frequently overlooked unless the patient is examined in daylight or when the body is warm (GELFAND). Inspection under oblique light is of great help. The macules are not

of the roseola type but show up as black spots (MURRELL). This fact was emphasized also by SCHROEDER and by SCHEUBE as a result of their observations of African natives, and SCHROEDER characterized the *roseola in blacks "as an intensification of the normal colour of the skin"* This phenomenon is due to the fact that the rash results not only from hyperaemia but also from the increased activity of the melanoblasts (SPENCER)

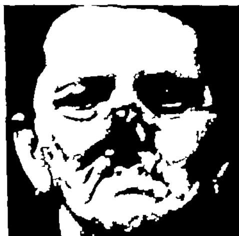
Papular lesions though seen in whites, are distinctive of syphilis



236. Huge circinate nodular ulcerated late syphilis.
(New York-Skin & Cancer Unit Dir M B Sulzberger)

in the Negro (HAZEN) in whom they show very significant variations The papules may be covered with silvery scales closely resembling psoriasis (psoriasiform syphilid) or the central portion of the papule may be hyperpigmented and surrounded by a squamous margin (*colerette de* BIETT) Often of miliary or follicular type the papules may remain discrete, but there is a noteworthy tendency toward grouping and clumping The latter may consist of a number of small papules around a larger one forming the corymbose syphilid or

presenting a fungating berry like appearance (*frambesiform syphilid*) In another configuration they coalesce to form circinate, polycyclic, gyrate, and annular arrangements, which are particularly characteristic of the late secondary stage of syphilis but may also occur in the early period. The circinate variety was first named *syphiloderma papulatum circinatum* by ATKINSON who originally called attention to it, and later was designated annular papular syphilid by FOX and GILCHRIST



237 Tertiary syphilitic "gangosa"

(Hartel - Münch)

The circinate lesions are mainly on the face, especially around the orifices, mouth, ears, eyes, nostrils. According to STOKES "they appear as fully developed rings as perfect as drawn with the compass or with segments missing where they cross intervening structures as the lips" The circinate syphilid is prevalent in the Negro (HAZEN ZIMMERMANN, TURNER) and is not only the most significant racial variation in syphilis but was considered by FOX as "*the most striking dermatological peculiarity of the Negro*" YOUNG reported that "the annular or horseshoe secondary lesion is also a curiously common type of late secondary manifestation in the African" in whom he "also found more than once a varicelliform syphilitic rash" which HAZEN called

a very common florid secondary lesion in the Negro LACAPÈRE saw *bullous lesions* on two occasions in African natives

Another topographical peculiarity is the occurrence of papules on the palms and soles This type of lesion, often squamous in character may be the only clinical manifestation of the disease and, as DEXTER has recently reiterated, thus may be confused with other dermatologic al conditions which occur in those areas such as dermatophytosis Moist papules *condylomata* are exceedingly common in coloured patients. HEINZ considered them to be the dominant form of secondary manifestations in African natives among whom DE MELLO also



238 Gumma of the upper lip with destruction of the soft palate

found them frequently They are more prevalent in women, and HAZEN stated that "*nearly every Negro woman with florid syphilis is affected by this type of lesion*" According to STOKES, the coloured woman holds an unenviable record in this regard these infectious lesions being 3 5 times as common as in the white male and 3 times as common as in the coloured male and more than twice as frequent as in the white female" They are found predominantly in the folds of the vulva, and in both sexes in the groins the inner aspects of the

thighs, and particularly the perineal, anal, and perianal regions condylomata are not usually found in the axillary and submammary folds (HAZEN) but they have been observed in the interdigital webs of the feet (STOKES). In African natives "the condylomata of the anal region tend to assume giant form" (LEES). More frequent, also in the Negro are the pustular papular pustular and the small pustular eruptions which often resemble smallpox (HAZEN) and have been confused with that disease (STOKES). About the South African natives



239 Residual grouped and gyrate keloids in late syphilis.

REITH FRASER stated that "by far the most common secondary eruptions are (1) *the roseolar syphiloderm* (2) *the severe pustular eruption*, and (3) *the rupial eruption*" *Ulceration* followed by crust formation, may transform large pustular lesions into impetiginiform syphilid which was frequently seen by JEANSELME in the Far East. *Crusted lesions* about the scalp face forehead nose, and mouth were often noticed by one of us (S) among syphilitics in Mexico Dr MELLO mentioned that impetiginous secondary syphilis affecting the nose,

the angles of the mouth, the area below the arm pits and the back of the elbow occurred in Africans.

Syphilitic alopecia seems to be relatively uncommon in coloured patients according to STOKES it is half as common in coloured females as in white females in whom it is less frequent than in white males.

Special consideration has to be given to a peculiar white scaly form of baldness in African natives (LEES) which is called *white head*" or by the natives themselves *witkop* or *dikwakwadi*" It may be considered as a syphilitic manifestation of local significance



240 Serpiginous nodular lesions with residual leukoderma at the elbow in late syphilis

It was reported first by MACARTHUR and THORNTON in 1910 as a frequent occurrence in South African syphilitics Although it was thought to be a manifestation peculiar to heredosyphilis, REITH FRASER reported that he "met numerous examples in the secondary stage of acquired syphilis"

The condition was described by M[illegible] A[illegible] [illegible] follows "It is [illegible] peculiar syphilid affecting the scalp The pustules [illegible] isolated and scanty at first, but they gradually increase and tend to coalesce forming thick whitish crusts [illegible] varying sizes. In some cases the head becomes [illegible] giving the appearance of [illegible] solid white cap There is often complete loss of ha[illegible] but in cu[illegible] cases a partial re-gr[illegible]

place." REITH FRASER stated: "The denuded, polished, thin, or atrophic condition of the skin of the vertex is well known as "*kaalkop*" (which means baldness). According to him "the condition occurs only in natives suffering from syphilis male and female alike, and it has never been met with affecting Europeans"

Because it resembles conspicuously the clinical features of favus there was a sharp controversy about it between MACARTHUR and REITH FRASER on one side, and MITCHELL and ROBERTSON on the other The latter authors denied that syphilis was the cause of the



241 Grouped hyperpigmented scars in late syphilis

condition and classified it as of mycotic origin. They succeeded in growing from the lesions fungi which appeared to be closely allied to the Achorion schoenleini of favus However most investigators seemed to be inclined to favour the syphilitic character of "witkop" (See also page 137)

With the occurrence of early syphilitic *mucous membrane lesions* of mouth and throat in coloured patients, experiences vary CARTER did not observe a single mucous patch in 231 coloured syphilitic patients BAETZ found them not nearly so common as in whites ZIMMERMANN saw them about twice as frequently in whites as in the

Negro but HAZEN considered them "probably more common than in whites" According to JEANSELME mucous patches were an extreme rarity in the Far East on the other hand, they were reported seen as frequently in African natives as in Europeans by LACAPÈRE and others. LACAPÈRE explained the erroneous opinion that the mucous patches were rare by the fact that the native people in North Africa only exceptionally ask for medical help for such lesions and stated that they were frequently detected when patients came for other examinations The mucous patches of lips and tongue often ulcerate, a fact which was also reported by LAMBKIN based on his observations in Uganda. According to STOKES coloured women present the highest proportion of these infectious lesions, and they are particularly subject to mucocutaneous relapses, an opinion which was not shared by HAZEN, however Whatever the frequency of mouth and throat lesions may be, it seems that, in contrast to cutaneous syphilis the clinical characteristics of those lesions are not notably different from such lesions in the whites.

Pigmentary and atrophic changes are the only definite exceptions to the rule that secondary syphilids involute without trace (STOKES). It may be stated, however that in those individuals possessing a fibroblastic diathesis, which is encountered more frequently in non-whites particularly Negroes, some forms of secondary syphilis may result in *keloid formation* The pathogenesis of the pigmentary changes has been the subject of an extensive controversy among students of the problem (TAYLOR) Macular as well as papular and pustular eruptions may be followed by depigmentation (*leukoderma*) hyper pigmentation (*melanoderma*) or a mixture of depigmented and hyperpigmented zones the melanoleukoderma" of FOURNIER which was reported by LACAPÈRE The area predisposed to these changes is around the neck, whence came the French term *collier de Vénus*' The dyschromias are of great diagnostic importance as they are highly indicative of previous syphilitic infection when no other signs or stigmata of the disease are present Because of the natural colour depigmentation is of course, much more conspicuous in non-whites than in whites particularly the residual pigmentary changes around the orifices of the face, may offer considerable cosmetic difficulties Atrophic changes following secondary eruptions the so-

called macular atrophy are likewise more noticeable in non-whites It may be mentioned finally that "*pruritus* unusual in white patients is not infrequent in coloured patients, especially in association with the follicular syphilid" (ZIMMERMANN).

2. *Late Syphilis*

HAZEN states that "late lesions of the skin, bones and eyes are much more apt to develop in the Negro than in the white" but the higher



242. Juxta-articular nodules in late syphilis.

incidence in Negroes is not brought out by the figures given by ZIMMERMANN, who found in a group of 887 patients with tertiary syphilis late manifestations in 421 whites and 466 Negroes. According to TURNER the "skin and mucous membrane lesions occurred with about equal frequency in the two races" Reports about tertiary syphilis in natives of tropical countries vary considerably and it has to be stressed, as it was previously that some investigators very likely confused late signs of yaws with those of syphilis. LACAPÈRE wrote that *tertiary forms were the most frequently* observed in North African natives. For this fact h. gives the explanation that the natives do not consult a doctor before the lesions interfere with their daily

work. On the other hand BARKHUUS reported from Ethiopia "Tertiary lesions are rather rare, most likely due to the fact that life expectancy is so low" As much as the opinions conflict regarding the prevalence of tertiary syphilis so do they differ on which types of late manifestations are most common. Often various organic systems are affected in the same individual VONDERLEHR and co-workers studied 369 male Negroes with untreated syphilis and found among those with tertiary manifestations 36 patients with bone and joint lesions 2 with skin lesions, and 8 with both skin and bone and joint lesions. ZIMMERMANN found bony structures affected twice as often in Negroes as in whites, while he saw cutaneous lesions 74 times in 421 white and 68 times in 466 coloured patients with late syphilis. LACAPLRE found skin lesions the most frequent late manifestations of syphilis in African natives. Of 2,702 with tertiary syphilis more than 1 100 had skin, 790 bone and joint, 505 mucous membrane, 280 subcutaneous gummatous lesions Of the various types of skin lesions, the gummatous type is much more prevalent among Negroes—according to HAZEN six times as frequent as in whites Otherwise all forms of late skin lesions, such as papular nodular circinate ones occur in coloured syphilitics as in whites Some peculiarities have been noted however TURNER for instance, pointed out that the lesions seen in coloured patients seemed to be more advanced than in whites, which, he thinks is due probably to the tardiness with which the former seek treatment, rather than to any racial difference" While MACARTHUR spoke of "very slowly progressive tissue destruction in syphilis in South African natives it still seems that in the Negro the gummata have a greater tendency to break down to form ulcerations followed by the development of extensive crusts, of vegetations, and of papillomatous lesions The formation of keloidal scars is quite common Probably the majority of all scars resulting from tertiary lesions present considerable pigmentary changes either of the depigmented, hyper pigmented, or the mixed type with leukoderma in the center and hyperpigmentation in the periphery

Special attention has to be given to a somewhat unusual condition, the *juxta-articular nodules* because they are not infrequently seen in natives of tropical countries and as JEANSELME stated although their nature is not completely understood, one knows that they can be a

manifestation of syphilis According to KALZ and NEWTON they may be defined as painless, slowly growing subcutaneous fibrous nodules often symmetric in their distribution and if untreated, of long duration. They are situated in the vicinity of a joint, especially of the extremities and are not attached to the skin or related to bursas or tendons. Sites of predilection. are, in order of frequency elbows knees, tibial tubercles, sacrococcygeal area and costal cage" They are produced by heterogeneous and manifold causative agents. BERTIN, who was first to report such lesions from Guadeloupe (1778) and from Santo Domingo (1786) thought they are caused by a combination of yaws and syphilis. In 1891 LUTZ wrote about similar findings in Honolulu where he observed them repeatedly in natives and foreigners" some of those affected had leprosy some had not, but all were more or less suspect of syphilis. Without knowledge of LUTZ communication, JEANSELME (1899) saw them in natives of Indo-China and fully described them, coining the current generally accepted designation of juxta articular nodules. It was JESSNER and co-workers who succeeded in proving by animal inoculation that syphilis is *one* of the infections in the course of which these lesions occur Yet there can be no doubt that in tropical and sub-tropical areas with high incidence of yaws this disease is the paramount cause, an opinion which was recently confirmed by CHAMBERS, who reported from the West Indies on 128 patients with juxta-articular nodules with neither history nor evidence of syphilis. The original conception that these nodules occur only in the tropics mainly in natives, but also in whites who live there, could not be maintained since in 1920 DE QUERVAIN presented a case in Switzerland of a syphilitic patient born there and who had never left that country and previously SELLEI, using the term *tumor fibrosus syphiliticus* had reported similar findings in four soldiers from Bosnia. Thereafter a number of cases have been reported from other non-tropical regions of Asia, from Europe, and also from the United States and Canada. It seems that most of the cases reported from the United States were in coloured people, and FASAL recently stated "that he has seen juxta-articular nodules of syphilitic origin only in Negroes"

3 *Congenital Syphilis*

The cutaneous manifestations of congenital syphilis hardly require any special discussion, as their characteristics are similar to those of the acquired form. (See also the chapter on Bejel)

COMMENT

An exhaustive discussion of the possible causes of racial differences in the prevalence and manifestations of syphilis is not feasible within



243 [illegible] a non venereal syphilis in Africa. Secondary stage revealing *condylomata lata. (There is also an intertrigo.)*

([illegible] London)

the framework of this chapter A short review of the theories that have been presented as explanation of the differences seems appropriate however

The hypothesis that different strains of Treponema pallidum exist has been postulated by LEVADITI and MARIE but agreement on this controversial issue has never been reached. It appears unlikely if not impossible that different strains can be causative agents when

people of different races live in areas in which there are hardly any barriers against interracial sexual contact.

In discussing the problems in question, LEWIS wrote "Differences have been established between the Negro and the white man in regard to both the prevalence of syphilis and its clinical and pathological manifestations, but it is questionable whether these differences are fundamentally racial in nature or whether they are due to differences in the histories of the races in regard to contact with the disease and in the operation of external, chiefly social factors" In other words, two factors have to be considered Inherited biological factors and environmental ones A similar opinion was expressed by KÖNIGSTEIN and WERTHEIM who said "The geographical, climatic, and ethnologic factors play a role in syphilis first, regarding the frequency and, second, regarding its manifestations" Although racial peculiarities such as early sexual development with a tendency toward promiscuous intercourse, have been blamed for the greater prevalence of syphilis among Negroes (QUILLIAN CORSON) no scientific proof exists for this opinion, and LEWIS considered it "doubtful that Negroes are ten times more promiscuous than the white people to account for ten times more syphilis as has been claimed for some groups of coloured people" Rather than racial factors, socio-economic factors have been considered by most students of the problem responsible for the higher incidence of syphilis among coloured people.

MCHATTAN spoke of close crowding poor clothing and food, and failure to observe the ordinary laws of hygiene" MCNEILL stated that "the occurrence of syphilis among white people of the same social class as the Negroes would seem about the same as among Negroes" The socio-economic viewpoint was also emphasized by FULLILOVE and by SAMPSON in their replies to SMILLIE who unfortunately characterized "syphilis in the United States as primarily Negro problem" More recent elaborate studies of the prevalence of syphilis in Georgia by BOWDOIN and his co-workers and by W[illegible]NER and his group also seemed to indicate that "the disparity of the white and non-white rates was associated with differences in socio-economic conditions"

And now how are the differences in clinical manifestations to be explained? In his classical study about skin diseases in the Negro Fox called attention to the anatomical peculiarities of the Negro skin, such as deeper pigmentation, greater thickness, and a more highly developed glandular system. The fibroblastic diathesis, expressed by

the tendency to keloid formation, the increased activity of melanoblasts with hyperpigmentation and differences in the susceptibility of various tissues are recognized as distinct racial characteristics in Negroes It cannot be denied that these biological differences play a role in the course and clinical manifestations of syphilis because these differences are evident in coloured people who live in an environment, climatic or socio-economic, similar to that of the white population The explanation of differences by racial factors has not been acceptable to some investigators and the very existence of noteworthy differences has been denied by others. GRAU-TRIANA, for instance, stated that syphilis is more or less uniform everywhere" In this connection the vigorous fight of MONTEL against the conception of *exotic syphilis* the term coined by French syphilologists in the beginning of this century and used mainly during its first quarter merits attention. MONTEL observed syphilis in tropical natives for more than forty years Although he recognized some biological, anatomical and physiological variations in the coloured skin, he considered these racial factors minimal and negligible as causes of the peculiarities of syphilis in the tropics but the environmental factors as decisive He stated If the men of the white race were subjected to the same social conditions as the coloured races in the tropics the manifestations of their syphilis would certainly be comparable" and he proclaimed the thesis "Syphilis is one and identical everywhere.

Finally it has to be taken into consideration that syphilis has changed its character (FINGER), because of various not yet determined factors and because of improved treatment methods and improved control measures. For example, DECROP recently emphasized the fact that the destructive forms of the disease which were described by LACAPERE in Morocco less than one generation ago are not seen any longer as the result of the vigorous campaign against venereal diseases and the more widespread application of more efficacious therapy

It must be left to future investigation to clarify the numerous unsolved problems.

After this chapter was finished the following interesting article which deals with a related topic came to our notice CLARK C H V Some comparisons of skin diseases in different climates and races, *J Trop. Med* 54 49 (March) 1951

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CHAPTER 6

BEJEL[1]

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DEFINITION

It is a striking feature of treponematosis that, unlike most other diseases it has been given a multitude of different names. This fact is a witness to its universality and is not without some bearing on the nature of the disease. So many names have been given it that some writers have called it the "disease of one thousand names Certain authors have made collections of these names numbering several hundreds. Sometimes treponematosis has been called by descriptive names such as *framboesia* (raspberry) *sibbens* (berry) *pastuhs bubas pinta* sometimes by transliterated native names such as *yaws* (Africa) *irkintja* (Australia) and *bejel* (Syria) sometimes by fanciful ones like *syphilis* or the disease of *St Job* Sometimes it has borne two names simultaneously in the same country one to describe its adult acquired venereal form and the other for its non-venereal, childhood-acquired form. Thus in the Balkans there was *syphilis* and *skerljevo* in Australia *kirkal* and *irrkintja* and among the Arabs *frangi* and *bejel* Sometimes a particular manifestation has been dignified with an individual name such as *gangosa* in Guam and *pinta* in Mexico.

HISTORY

Bejel was presented in 1928 as a spirochetal disease due to *T pallidum* a variant of the "syphilis-yaws" treponematosis found among the Arabs of the Syrian desert. Subsequent articles established the juvenile character of bejel, its high incidence in the Bedouin communities its uniformly positive

[1] This is an excerpt from HUDSON's book on Treponematosis with permission of Dr HUDSON, Ohio University Athens, Ohio Dr HENRY A. CHRISTIAN and the medical Department of the Oxford University Press Inc., New York.

serological reactions, its ready response to anti-syphilitic treatment and its numerous points of identity with yaws. Darkfield studies showed that it was due to a treponeme identical with *T. pallidum*. In 1937 the information about bejel was summarized and it was stated that the Arab word, bejel, had been introduced into the literature solely to distinguish this non-venereal syphilis from the venereal implications associated with the word syphilis as ordinarily understood.

Whence bejel came is unknown. The Arab word which thus is transliterated is probably an old form meaning "sores."

SYMPTOMATOLOGY

The clinical course of bejel is briefly as follows. At some time in early life the Bedouin child contracts bejel from some other child in the acute stage of the disease. The spirochaete usually is passed from host to host by immediate, non-sexual contact, and the transfer is favored by general uncleanliness, total lack of segregation and the succulence of the mucocutaneous lesions. Possible auxiliary factors in contagion are the use of a common drinking bowl, the habit of kissing and fondling children and the presence of the domestic fly, the louse and the flea. Lesions often appear first in the mouth but are soon followed by moist papules in the folds of the skin and by drier lesions on trunk and extremities. Treponemes are easily demonstrable in great numbers in all these lesions. A roseolar eruption has been observed but is rare. Late lesions consist of ulceration and erosion of palate and bones which involve pharynx and often larynx, gummata of skin and subcutaneous tissues producing huge ulcers and cicatrices, osteoperiostitis particularly of the long bones with formation of sabre shins, adenopathy, juxta-articular nodules, hyperpigmentation, depigmentation, hyperkeratosis and alopecia. An adult who has escaped bejel in childhood, is likely to contract it later from a child, often his own. The course of the disease in the adult does not differ essentially from that of the child. Hypertension is virtually unknown in the Arab and he does not suffer from aneurysm; meningovascular syphilis, tabes and paresis are exceedingly rare. Bedouin women, who have had bejel, do not ordinarily transmit it to the fetus; abortions and miscarriages are not more frequent among them than among neighboring groups of women.

PATHOGENESIS

That bejel is treponematosis is established by the character of its early and late lesions, the quality of latency, the uniform presence of a treponeme indistinguishable from *T. pallidum*, the positive precipitation and complement fixation reactions and the favorable response to antitreponemal drugs. It is a juvenile disease, acquired non-venereally, existing almost wholly without regard to sex. It is found in both sexes and all ages and to the

same degree in the sick and presumably well components of the Bedouin population among them it is wellnigh universal.

It is noteworthy that as in yaws chancres are seldom, if ever observed in bejel, and there is no shame attached to the disease. A clear distinction is made by the clinic patients between bejel the *juvenile disease of the* Bedouins and franghi the venereal disease of the town. The semi-nomad Bedouin does not mind having bejel but he resents any suggestion that he might have franghi for he distinguishes their respective epidemiologies.

Bejel is indistinguishable from yaws in non-venereal juvenile acquisition, community wide dissemination, absence of chancres and congenital transmission morphology of the skin lesion, relative escape of the eyes, the cardiovascular system, the central nervous system and the viscera, the lack of constitutional disturbance the lack of infantile dystrophies the failure to impair fertility and virility and the presence of gangosa juxta articular nodules and patchy depigmentations. Both bejel and yaws tend to disappear rapidly when brought into contact with civilizing influences. In both the problems and the methods of treatment are the same. On the other hand bejel is indistinguishable from syphilis in its constant involvement of the mucous membranes in the early stages in the occasional finding of alopecia, in many of its general pathological aspects and in its extra-tropical geographical location. One can either discount all resemblances to syphilis and say that bejel is yaws modified by a desert climate, or one may identify it with syphilis as seen under the epidemiological conditions of a semi-nomad and desert people. In fine, there is no clear-cut differential between bejel and yaws or between bejel and syphilis. It is a variant of treponematosis one of those transitional forms which prove the essential one-ness of this versatile disease of man.

The parallelism between congenital syphilis and early bejel is striking, notably in the apparent resistance of the cardiovascular system, but there are obvious differences for example, meningitis is rare in bejel though common in congenital syphilis, and the bejel child does not have the Hutchinsonian triad or the facies of congenital syphilis. There may be those who looking at the similarities, would like *to think of* bejel *as a* special form of congenital syphilis. Indeed, this view might be defended were it not for the one factor in bejel – its *contagious* nature. It seems incontestable that the Arab child "catches" bejel from some other child who already has it. Bejel affects together the children of a family and occasionally includes a father or mother should they have escaped it in early life. This epidemiological fact cannot be fitted into the concept of a congenital pattern (*Journ. Med. Libanais Beirut* 1951)

There have been various attempts to "explain away" bejel. Some have claimed on ipse dixit grounds that bejel is just ordinary syphilis and its nonvenereal feature a myth others insist on regarding it as a third disease,

different from both syphilis and yaws. These dislike the suggestion that the cause of bejel is *T. pallidum* and suggest that it is caused by still a third treponeme. It would suit them better if the parasite of bejel had been given another name. Thus one comment runs: "I notice you state that this condition is caused by *T. pallidum* and I am wondering how you can prove that this is so beyond the fact that it has the same morphology as pallidum. It seems to me it is a matter of opinion whether the spirochaetes causing yaws, syphilis and bejel are one and the same, or whether they are good species. The fact that they are indistinguishable in morphology does not prove that they are not good species" (personal communication). The reply of course that bejel is caused by *T. pallidum* is exactly the same as the proof that syphilis is caused by *T. pallidum*, *viz.* identification of the parasite in the dark field, constancy of serological reaction, constant presence of certain definite fundamental pathological processes and response to specific treatment. Suppose the question were turned around, how could one prove that bejel is not caused by *T. pallidum*?

If, as seems reasonable, syphilis and bejel are both caused by the same parasite, a logical corollary would be to regard *T. pallidum* as the cause of yaws; also for bejel demonstrates that the environment produces many of the well-known differences between syphilis and yaws and a rapidly diminishing residue of differential points remains. The significance of bejel is that it places fresh emphasis upon the influence of environmental factors in the production of the various clinical entities which make up treponematosis. Bejel, to those who have described it, has never been a disease sui generis. When it has served its harmonizing role among the various clinical entities of treponematosis, the word bejel should pass into medical history along with the words sibbens and radesyge.[1]

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POST SCRIPTUM ON NJOVERA

In the Lancet of March 1951 WILLCOX has described an endemic syphilis of Southern Rhodesia, called "*njovera*". It is usually contracted in childhood. A primary lesion is not often seen, but a "throwback" is

(1) Our knowledge of the form of treponematosis known as bejel is incomplete and it may be well to close these tentative remarks with the words of EVAN THOMAS — "Syphilis is an extraordinarily complex and varied disease and one is never justified in making generalizations about it without abundant evidence" (*Journ. Med. Liban. Beirut* 1951)

occasionally observed e g in the case where a mother while nursing her baby had a large sore on a nipple and enlarged indolent axillar adenitis with typical secondary lesions. Njovera lesions are typically present within the mouth or on the lips and accompanied by cervical adenitis and laryngitis. The external oral lesions are often confused with angular stomatitis. The next most common secondary lesions are condylomata



244 Gummatous destruction of the nose in late njovera a non- enereal syphilis, which is most probably identical with bejel. (See also chapter 2.)

lata, from where *T pallidum* may be obtained without difficulty Secondary lesions of the body are much less often seen, they are usually frambesiform but diffuse and scanty The serum tests for syphilis are positive and njovera responds to antisyphilitic therapy Tertiary lesions may not always be associated with njovera, although the African may call gummata of the nose and soft palate njovera. *A comparison of njovera with bejel in Iraq showed that they are similar if not identical It is believed that both conditions are in fact syphilis* (WILLCOX)

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id *Textbook of venereal dis* 1950

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CHAPTER 7

YAWS (FRAMBOESIA PIAN)

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Yaws (English), pian (French) or framboesia (German) are names for a disease, widespread in the tropics, that occurs almost entirely in indigenous peoples. Its synonyms include *bouba* (Spanish) (also applied to South American cutaneous leishmaniasis, as is *pian bois*) and many local names which often differ with the type of lesions present. (The term pian originates from the Caribbean name "epian".)

DEFINITION

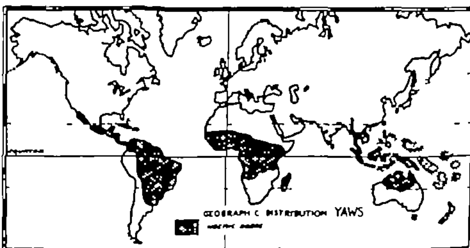
Yaws is a spirochaetal disease which starts with a non-venereal primary sore at the site of infection. In about 3 weeks this is followed by a generalised secondary eruption of moist papillomata and perhaps other secondary lesions of the bones, palms or soles. After a symptom-free period of some years, destructive tertiary skin and bone lesions may develop. There is no evidence of serious damage to the heart or central nervous system or of transmission to the second generation.

HISTORY

Its antiquity is probably considerable. It was in Africa before the slave trade to America started and may have been taken to America by that movement. It was probably present in Oceania and Australia prior to European discovery (HACKETT, 1936).

EPIDEMIOLOGY

Although yaws chiefly occurs (Fig. 245) in warm moist, tropical climates at lower altitudes, insanitary conditions as regards habits, clothing and housing are important Yaws occurs in most countries in the tropical belt except in arid or mountainous regions. Its incidence in only a few localized areas in India and China is exceptional *In some tropical* countries where social habits are advanced yaws may be practically absent but in such areas syphilis is often prevalent (Ganda tribe in Uganda). In the tropics high rainfall is often associated with high yaws incidence Secondary yaws skin lesions are most frequent during



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rainy seasons and are less frequent during dry seasons this must be taken into account when surveys are made (HARDING 1949). New infections may be favoured by moist skins but a large proportion of secondary skin lesions are relapses. Thus the effect of climate might well depend on changes in the body harbouring the spirochaetes or changes in the spirochaete already in the body An outbreak (SCOTT 1933) of 340 cases of yaws in a Witwatersrand (South Africa) mine was made possible by the humid conditions underground No yaws occurred among surface workers. It is also noteworthy that 7 cases of yaws in Europeans working in the mine concerned developed the

same type of exuberant secondary lesions as did the African cases. HARDING (1949) stresses the relation of the incidence of yaws to low social status and defective hygiene.

Transmission must be mainly by contact. There is usually abundant opportunity for this in scantily clad or naked peasants. HARDING (1949)



246. Primary yaws on the antero-medial surface of the right ankle.

believed that in Sierra Leone yaws was a house disease since many infections probably resulted from the close contact at night of occupants sleeping in the same hut. Most initial yaws lesions are on some exposed part of the body, e.g. the limbs and especially the leg below the knee (50—90 per cent.). Injury probably offers entry for infection but in a number of cases this occurs in some pre-existing ulcer. YAMAYAMA (1928) stated that the yaws spirochaete does not survive for more than a few hours outside the body, hence infective contact

probably cannot be remote. LUMSDEN (1947) reports the active motility of *T. pallidum* for more than a week at room temperature after removal



247 Typical secondary yaws in the left axilla

from the body provided drying was avoided but the survival of these organisms was not checked by their ability to infect.

The possibility that small flies (e.g. *Hippelates* species in Jamaica



248. Typical secondary plantar yaws.



249 Circinate secondary yaws resulting from irregular healing



250. Scars of second ry yaws together with healing relapsed secondary yaws. Often the scars are much less obvious or even not recognizable



251 Hyperpigmented secondary macules with desquamating margins on the flexor surface of the right forearm.

(KUMM & TURNER, 1936) or *Musca sorbens* (Africa, LAMBORN 1936) by feeding at infectious secondary lesions, may mechanically convey spirochaetes to uninfected individuals within an hour or so has been demonstrated but is probably not the usual means of transmission.

In highly endemic yaws areas nearly the whole population is infected by adolescence, those few that are not are often infected later by their own children. Infection is unusual in the first 18 months of life. Often by 5 years of age the infection rate is 50 per cent and by the age of 15 nearly 90 per cent. of the population may have been infected. A survey of 100 apparently healthy adult males between the ages of 18 and 35 in a yaws area in Uganda, by the Kahn reaction showed that over 80 per cent. had positive sera although most of these were infected years previously (HACKETT 1947)

AETIOLOGY

The causal organism, *Treponema pertenue* CASTELLANI 1905 is morphologically indistinguishable from *T pallidum*. Neither organism has at present, been satisfactorily grown on sterile media. Animal inoculation (TURNER, 1937) with these two spirochaetes results in constant differences which indicate that the organisms are different. This has been supported by cross immunity experiments in animals (SCHÖBL, 1928) and observations in yaws and syphilis areas in the tropics. TURNER *et al* (1947) have found in rabbits less cross immunity between the spirochaetes of yaws or syphilis and *T cuniculi* (rabbit spirochaetosis) than between those of yaws and syphilis themselves. Cultivation of the spirochaetes in fertile eggs may allow closer study of antigenic structure after which the relationship of the organisms in this group might be more clearly defined. This knowledge may be preceded by that obtained from the study which is now being undertaken in the U S A of the immobilization of spirochaetes by specific antisera.

RELATION OF YAWS AND SYPHILIS

HUDSON (1946) considers that one spirochaete, the *Treponema pallidum* of syphilis, with no static varieties is the causal organism of syphilis, yaws, *bejel* (non-venereal syphilis of Arabs HUDSON 1937) and *pinta* (a patchy depigmentation of the skin in South and Central America see page 307) STANNUS (1936) however and many who have studied

yaws, regard yaws and syphilis as two separate diseases Teams of the World Health Organization are at present studying all these spirochaetal diseases.

The pathological changes (FERRIS & TURNER, 1937) in the two diseases have no reliable differentiating characters and many secondary and tertiary lesions are much alike At present no indisputable evidence of damage to the heart or central nervous systems (SLAMET SUDIBYO, 1939) has been found. Congenital infection has not been observed even when the mother has active secondary yaws at the time of the birth (BAERMAN & SCHÜFFNER, 1912) Secondary yaws lesions on the buccal mucous membranes, contrary to statements in



252. Thick scabs in secondary yaws.

many tables of differentiation, do occur in yaws—in 6 per cent of 152 cases in Uganda (HACKETT 1939 see also SCHÜFFNER, 1907 and BAERMANN 1911).

In Uganda the incidence of initial genital lesions in young adults and the absence of yaws in children in the Ganda tribe in contrast with the high incidence of generalised papillomatous yaws lesions in children and the absence of initial genital lesions in young adults in the Lango tribe are very suggestive that yaws and syphilis are two separate diseases (HACKETT 1947)

Experimental inoculations in *Macacus cynomolgus* in the Philippines (SCHÖBL & HASSELMANN 1932) and in rabbits (PEARCE & BROWN 1925 and TURNER, 1937 and 1947) indicate the separate identity of the

(KUHM & TURNER, 1936) or *Musca sorbens* (Africa, LAMBORN, 1936) by feeding at infectious secondary lesions may mechanically convey spirochaetes to uninfected individuals within an hour or so has been demonstrated but is probably not the usual means of transmission.

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and VAN DER SCHAAR (1933) inoculated yaws spirochaetes into 53 cases of neuro-syphilis with success in only 2 cases. Further studies are required.

SYMPTOMATOLOGY

The disease starts with the entrance into the body of the *Treponema pertenue* most probably through some break in the skin. *The incuba-*



254 Secondary yaws on the face of patient with genital syphilitic chancre contracted two months after the appearance of yaws.
(Carman—Kenya)

tion period is probably 3–4 weeks. The *primary lesion* (mother yaws maman pian, bouba madre) (Fig 246) at the site of infection starts as a small papule and develops into a papillomatous area 2.5 cm. or more in diameter It is pinkish yellow and irregularly coarsely granular At its most active stage abundant serum containing many spirochaetes

exudes from its surface this dries to form a scab which is repeatedly shed and reformed Since the primary lesion occurs mainly on an exposed part of the body and most frequently on the lower leg it is probable that minor traumata provide the skin breech through which infection enters. Vegetation, dead or living, could easily be the instrument of the injury Yaws infection in an already existing ulcer (5–10 per cent) may give rise to a more luxuriant initial lesion. When such lesions heal the ulcer may still remain this may be the source of reports of initial or secondary lesions persisting and developing into tertiary ulcers It is possible that an obvious primary lesion does not develop in some cases but this is probably very unusual since most patients can indicate the site of the first yaw MONTEL (1951) however stresses that ulceration is characteristic of the initial lesion.

Evidence of general infection even preceding the earliest secondary lesions may be shown by pyrexia, malaise, headache rheumaticky bone pain and lymph adenitis, though other causes of these may also be present (BOTREAU-ROUSSEL, 1938)

In 3 weeks or more after the development of the primary lesion, usually before it has healed the *secondary skin eruption* appears This may be of two broad types the *typical* which consists of papillomatous lesions similar to the initial lesion and the *atypical* in which the underlying pathological changes are less intense though still of the basic character of the typical group

The *typical secondary lesion* starts as a papule and may enlarge up to an area 50 mm in diameter The surface (Fig 247) is of medium to coarse granularity from the epithelial hypertrophy Its usual colour is yellowish tinged with red by dilated capillaries. During activity the clear serum which exudes from the surface dries to produce a temporary surface glaze Flies attracted by the moisture may irritate the lesions. As activity subsides a yellow scab forms which is soon discoloured by adherent debris and may reach considerable thickness (5–10 mm)(Fig 252) In anaemic children the surface of the lesions may be eroded Variations in the appearance of typical yaws result from healing progressing more rapidly at one edge of the lesions so that circular semilunear and even linear shapes may result (Fig 249). This group of lesions comprises the "pianomes" of MONTEL (1944b). Since there is little epithelial loss scarring is slight or absent After healing

there may be some increased pigmentation but this fades and finally the only alteration may be some slight loss in skin elasticity (Fig 250)

These typical lesions, from two or three to hundreds, may occur on any part of the skin although in different cases they might be more numerous in some particular region, *e g* face or limbs or chest. Often



255 Groups of acuminate papules in secondary yaws.

the scalp and trunk are less involved. During the stage of scabbing itching is very frequent.

On the muco-cutaneous areas of the lips (Fig 253), inner surfaces of the lips, the hard and soft palate, yaws lesions may occur in association with typical yaws on the skin, from which characteristic spirochaetes may be obtained and which histologically resemble the skin lesions.

Such lesions away from the lips, have been observed in 6 per cent of 152 cases (HACKETT 1939)

The *atypical group* of secondary lesions the roseole planque" and planides of MONTEL (1944) may be regarded as lesions of less extensive pathological change Pigmented macules (Fig 251), usually with desquamating edges, are occasionally seen on the forearm and dorsum of the hand. Areas often serpiginous of fine desquamation (Fig 257) may sometimes be demonstrated especially after washing the skin and then stretching it. Small slightly horny papules 1—2 mm often in groups (Fig 255) may occur on the trunk, face or limbs These are sometimes called pian dartre especially when combined with desquamation (BOTREAU ROUSSEL, 1937) or follicular papular or lichenoid yaws (not to be confused with pityriasis pilaris) Larger papules, often umbilicated, may be observed on the skin in front of the kneejoint. These lesions are more frequent during the earlier part of the secondary stage and may even precede typical lesions

In a random group of patients with secondary lesions probably more than half are suffering relapse. The number of relapses that occur varies with the duration of the infection—but are most frequent during the first year or so After 2—3 years the relapses are less frequent. Skin lesions are not always most numerous with the first eruption In late relapses lesions are often most frequent about the lips, axillae, genitalia and anus—neither these nor secondary yaws lesions about the genitals in adults (Fig 256) resemble *condylomata lata* Typical yaws lesions may erupt, especially during relapses through the palms and soles (Fig 248) giving rise to much pain in Indonesia these are called *bubul* (See also Fig 258 259).

Other secondary skin lesions occur on the palms and soles There is a great variety of these lesions which may range from circular areas of superficial desquamation and slightly increased pigmentation, through similar areas of epidermal thickening with fissuring to larger often scalloped, areas of thickening and erosion (Fig 260) Obser vation of a large series of cases shows many comparable with in completely developed typical yaws lesions Many of these lesions are aggravated by using the hands or by walking thus the working efficiency of the patient may be reduced The dorsum of the hand is usually unaffected although the flexor surfaces of the fingers may be

involved. Healing is usually complete. The term "crab yaws" for palm or sole lesions is best avoided since it has been so loosely used. Onychia occasionally occurs. Other secondary lesions are dorsal



256. Typical secondary yaws about the genitals in an adult.

ganglia of the wrist and relatively painless effusion into the knee joints.

Another important group of lesions in the secondary stage is the bone lesions (HACKETT 1946 and 1951). Probably many yaws cases

during the secondary or tertiary stages develop bone lesions. MAUL (1918) found 20 per cent. of a small series. The characteristics of secondary bone lesions (Fig. 266) are multiple foci of cortical rarefaction and extensive periostitis, involving many bones, especially in children. In adults the rarefied foci are larger and the periosteal deposits less extensive. Considerable swelling, pain and tenderness result but destruction is exceptional. Polydactylitis and goundou (uni- or bi-lateral bony swelling of the nasal process of the maxilla: BOUTREAU-ROUSSEL, 1925) are secondary bone lesions. The early stages of goundou (Fig. 277) will subsid espontaneously or after therapy but late inactive lesions require surgical removal. In secondary bone lesions, as in those of the skin, healing is usually complete, but sometimes cortical thickening and bony expansion may result. Relapses also are frequent.

Evanescence, tendency to relapse and non-destruction are characters of secondary yaws. 2 to 3 years after infection (HACKETT 1946a) secondary lesions become infrequent and although relapse may occur years afterwards in a few cases the usual course is for a latent period to be entered upon. This *the latent secondary stage* may end by spontaneous cure or by the appearance of lesions of the tertiary stage. The usual symptom-free period between secondary and tertiary lesions may last many years but occasionally in children there may be only 2—3 years between infection and tertiary lesions.

The fewer lesions present at the time, destruction and resulting scarring and slower course of the *tertiary lesions* differentiates them from secondary ones.

Characteristic skin lesions are of two forms. In one an early subcutaneous induration breaks down to form a small abscess. Later this breaks down to a localised indolent ulcer with an irregular rather dirty base (Fig. 264). In the other (Fig. 269) an extensive superficial relatively clean ulceration with a yellowish coarsely granular base spreads at the edges or one edge while healing is occurring in the centre or at another edge so that extensive areas may be involved, up to 15 cm. Both these lesions heal by the growth of epithelium from the edge or central islands of epithelium. At first the thin atrophic scar may be depigmented but finally (Fig. 265) it is deeply pigmented. Crippling contractures may develop in those scars especially those related to joints.

Other tertiary skin lesions are those of the palms and soles. They are characterised by extensive thickening and erosion (Fig 262) and especially by atrophy and pigmentary changes (Fig 263) on resolution



257 Areas of desquamation in secondary yaws on the lateral surface of the right thigh.

which is slow To the atrophic pallid hand JELLIFFE (1950) has given the name *ghost hand* Differentiation from secondary palm and sole lesions is greatly helped by the presence of other tertiary lesions. This question needs further study (See BAERMANN, 1911 HALLENBERGER,

1916 GUTIERREZ, 1923 SMITH 1930 HERMANS, 1931 and 1939 and MONTEL, 1944 b) These tertiary lesions do not frequently occur in cases with bone lesions. Other lesions of the palms and soles, with pitting or fissuring and not due to yaws must be differentiated from those referred to above.

Other changes occurring in the tertiary stage are dorsal ganglion of



258 Secondary plantar yaws with hyperkeratosis and eroded pitting



259 Secondary plantar yaws with hyperkeratosis and desquamation.

the wrist and free fluid in the knee joints The Dupuytren-like contractures that are seen in patients with tertiary yaws lesions are probably not the result of yaws infection Patchy depigmentation of the skin unrelated to previous ulceration occurs in a few cases Its relation to *pinta* is undetermined (SMITH 1930 and see Fig 263 and page 301).

Bone lesions form an important group in the tertiary stage (HACKETT 1951) Often a single bone is affected and the lesions are usually few in number Well-defined cortical rarefactions (Fig 267) often containing debris ("gummata") most commonly about 5 mm, are characteristic. Periosteal deposits may form on the cortical surface (nodes) and the rarefactions may extend into them. Ulceration through the skin may follow this never occurs in secondary bone lesions



260. Secondary palmar yaw with hyperkeratosis, desquamation and fissuring. These are not infectious.

Occasionally diffuse and extensive changes are present. Healing is slower than in secondary stage lesions and residual changes are more marked.

Tertiary lesions of the hand and foot bones usually involve one or only a few bones and may result in absorption of segments of phalanges or ulceration through the skin. Deformity often results. Spontaneous fractures and joint lesions may occur in tertiary cases but never in

secondary ones. Nodes on the skull with rarefaction, bony thickening and ulceration only occur in tertiary cases as does the destructive naso-pharyngeal lesion, rhinopharyngitis mutilans or gangosa (Fig 275). Ulcerations of the palate with perforation (Fig 271) are probably minimal lesions of gangosa, but in advanced cases the nose, upper lip,



261 Secondary palmar yaw with much desquamation

anterior part of the maxilla and roof of the mouth may be missing (Fig 276). Clavicles may be thickened. Practically every bone of the body may be affected vertebral lesions have occasionally been reported. Sabre-tibia (boomerang leg kakki parang (Indonesia)) is often

observed in yaws communities but is probably only in small part due to yaws.

After some years during which tertiary relapses may interrupt a *latent tertiary stage* the disease may die out. Most tertiary lesions occur after puberty and in highly endemic areas most of the population in



262. Tertiary palmar changes with extensive thickening and erosion. Note Dupuytren-like contracture of the little finger

the 20—40 age group have positive serum Wassermann reactions.

Despite contrary statements it is highly improbable that primary lesions develop into ulcerative tertiary ones or that secondary change into tertiary lesions or that lesions of more than one stage are present at the same time

SAUNDERS (1951) discusses the incidence of cardiac and neural com-

plications in yaws and concludes that though they may occur their incidence is much lower than in syphilis. Changes in the cerebro-spinal fluid have occasionally been reported but they are usually of small degree and short duration. Maternal infections of the new-born child does not appear to occur. The lesions occurring most remote from the time of infection are the juxta-articular nodules (Fig. 272) and



263 I ruary palmar y w resulting in atrophy and depigmentation.

prepatellar bursal enlargement. The former may also occur in syphilis and in rheumatoid arthritis.

As regards the suffering of yaws from the time of infection until the secondary relapses have become infrequent, "rheumaticky" pain in bones during the day and night, malaise and gross discomfort accompanying the eruptions are the rule. Pain is marked in bone lesions

During latent secondary or tertiary periods, although no patently active disease may be present, aches and pains in the bones are frequent. In the tertiary stage much pain is associated with ulcers and bone



264 Spreading indolent tertiary yaws ulceration. A recurrence at the site of a previous tertiary lesion at the left wrist.

lesions but these are usually few in number. The individual thus suffers more severe pain for a longer time. Fissuring of any lesions of palms and soles is painful. Multiple or extensive tertiary skin

or bone lesions and resulting deformities may reduce the sufferer to a state of great misery. This is well seen in advanced gangosa. MONTEL (1949) has stressed the importance of tertiary yaws to the life of a community. GUIMARÃES (1950a) gives a good description of the clinical development of yaws as it occurs in Brazil.



265 Typical atrophic pigmented scars of tertiary yaws.

PATHOLOGY

From the primary lesions in which the spirochaetes multiply the adjacent lymph glands become infected and enlarged. Later a blood infection occurs and spirochaetes are carried throughout the body. They have so far only been found in the skin, lymphatic glands and



267 Well-defined cortical rarefactions, bony expansion and localized perioste al deposits intertiary yaws bone lesions.

← 266. Multiple small cortical rarefactions and extern e periosteal deposits in se condary yaws bone lesions. (Left w dist).

bones but there are no records of thorough search after autopsy. Minor changes have been reported in the cerebro-spinal fluid.

The primary lesions and typical secondary skin lesions are characterised by rough surfaced flat papillomata. On microscopic examination (Fig. 268) epithelial hyperplasia, depigmentation, cellular infiltration and oedema of epidermis and cutis are observed. Great extension downwards of the epithelial rete into the cutis is characteristic. The demarcation between cutis and epidermis is maintained but may be obscured by inflammatory cellular infiltration mainly of plasma cells.



268 Section of a secondary yaws papule showing epithelial hyperplasia (acanthosis) hyperplasia of the papillae, cellular infiltration and oedema (30)

This infiltration also invades the epidermis. Perivascular infiltration may be present but vascular changes are not usual. The superficial epithelial layers are swollen and the vessels are dilated. Spirochaetes are most numerous in perivascular tissue and in cellular exudates in the cutis and epidermis. In other or atypical secondary yaws skin lesions the basic changes are similar but less marked and the superficial epidermal layers instead of being swollen and oedematous are often a thick dense *stratum corneum*. This change is frequent in the palms and soles. In some lesions there is little thickening of the skin but the increased epithelial multiplication results in desquamation

(see MONTEL, 1944a FERRIS & TURNER, 1937). The pathological changes in the bone lesions have been reported by BOTREAU-ROUSSEL *et al* (1937) The main changes were thickening of the periosteum in which were small collections of lymphocytes and plasma cells. Vascular sclerosis laminar absorption and osteoclasis were also observed together with increased fibrous and plasma cell infiltration in the medullary spaces Giant cells marked bony destruction and spirochaetes were not found BOTREAU-ROUSSEL (1937) regards all bone lesions as secondary stage lesions.

Tertiary lesions occur in the skin and bones. At present there are no generally acceptable records of involvement of other tissues. Tertiary yaws skin lesions resemble tertiary syphilitic lesions very closely Although HALLENBERGER (1916) stated that the vascular changes characteristic of syphilis were absent in yaws FERRIS & TURNER (1937) found no evidence to support this.

But little data of the pathological changes of tertiary yaws bone lesions are available. Some writers are uncertain regarding their occurrence but there can be no doubt of their existence (HACKETT 1946b) The changes consist of necrotic foci, bony absorption, periosteal deposition and cellular infiltration. In one specimen spirochaetes were found.

DIAGNOSIS

In yaws endemic areas clinical diagnosis is simple. The attendance at clinics is largely of children with many visible secondary skin lesions In syphilis areas there is a corresponding attendance of young adults with genital venereal lesions and very rarely with lesions resembling typical secondary yaws skin lesions. Where both diseases are presen differentiation may at times be impossible especially in the tertiary stage Yaws is more likely to be present in individuals from country areas and syphilis in those brought up in large towns.

Spirochaetes are usually readily demonstrated by dark-ground examination of smears from active secondary lesions. The Wassermann, Kahn and similar non-specific tests are positive in all active cases and in over 80 per cent of some adult populations, 90 per cent. of whom will admit previous yaws infection. These tests are useless in differentiating yaws from syphilis or in supporting the yaws origin of a lesion

such as Dupuytren-like contractures since many cases with unrelated conditions, *e.g.* "cuts and sprains" may have over 80 per cent positive serum Kahns. At present final appeal would have to be made to animal inoculation and not everyone would accept the answer.

THERAPY

Early workers in Netherland East Indies (SCHÜFFNER, 1907 and BAERMANN, 1911) report satisfactory results following treatment with



269 Localized tertiary yaws ulceration.

mercury but this is not often used at present. The modern chemotherapy of yaws has followed that of syphilis both as regards substances and individual doses. Whereas in syphilis careful observation has indicated the total dosage of a substance required to produce serological cure, this has not been so throughly done for yaws. The chief practical importance of the treatment of yaws has been the benefit received by the community rather than by the individual. The effort has been to render the individual non-infective and thus to reduce the risk to others ("blanchiment"). Clinical cure by mass therapy has been the intention.

Recent recommendations in the Belgian Congo (VAN NITSEN, 1944) are for 6 weekly injections of neoarsphenamine followed by 6 injections of bismuth. In tertiary yaws twice the number of bismuth injections should be given with one month's rest between the 6th and 7th injections. Twenty four hours after one injection of neoars



270 Result of extensive tertiary yaws ulceration of the face.

phenamine (0 45—0 6 g) spirochaetes may no longer be found in secondary lesions and healing is usual after 2—3 injections. Sulpharsphenamine arsenoxide and other trivalent arsenical preparations and the pentavalent arsenicals acetarsol or stovarsol may be used.

Bismuth, as metal or salts may be given in doses of 0 1—0.2 g of the oxide, 0 06—0.2 g of bismuth sodium tartrate or 0.3 g of salicylate.

Attention should be paid to the condition of the mouth and with insoluble preparations care should be taken to ensure adequate mixing before use.

The Jamaica Yaws Commission (1935) used neoarsphenamine (0 12 g per kilo to maximum dose of 0 75 g) and bismuth salicylate (0 05 ml of 10 per cent. suspended in oil per kilo to maximum of 3 ml) They found that of all types of yaws 18 months after 4 weekly injections of neoarsphenamine 22 per cent. had relapsed and about 58 per



271 Perforation of the palate in a woman who ha already suffered destruction and collapse of her nose.

cent had negative serum Wassermann reactions. Eighteen months after 4 injections of bismuth salicylate the results were 19 and 57 per cent respectively Eighteen months after 6 injections of neoarsphenamine the results were 18 9 and 65 per cent. and after 6 injections of bismuth salicylate 24 and 62 per cent VAN NITSEN (1944) publishes data which show that in some cases very little more treatment is required to produce serological cure than to produce clinical cure

Recently antibiotics have been used DWINELLE *et al* (1947), in Haiti found that among 196 cases of primary and secondary yaws, 12 months after 1.2 mega units of penicillin sodium in water in 3 hourly

injections for 4 days, in 26 per cent. the serum Kahn reaction had become negative and remained so ("apparent cure") and in 63 per cent.



272. Juxta-articular nodes in tertiary yaws.

the Kahn titre had fallen to a low level and remained there together with no clinical relapses ("satisfactory progress") Although no severe toxic reactions were observed, about half of the patients re

ceiving this course of treatment had febrile reactions within 8 hours *of starting treatment* *Transient pyrexia was observed in about a fifth* of the patients 3—5 days later Temperatures were not taken after the two following treatments. Twelve months after the same dose of penicillin calcium in arachis oil and 4 8 per cent. beeswax in two equal doses 24 and 10—12 hours apart (125 cases in each group) the per centages for apparent cure and satisfactory progress" were 11 and 81 and 6 and 86 respectively The shortness of the last courses would be important in field work It is unfortunate that these results and those following neoarsphenamine and bismuth salicylate are not comparable. REIN *et al* (1950) using a total of 2.4 mega units of penicillin G in arachis oil and 4 8 per cent beeswax in twice daily doses for 2 days obtained 49 per cent apparent cures" and 45 per cent. "satisfactory progress after at least 12 months. The latest development of penicillin treatment is the use of a single depot injection of 1.2—2.4 mega units of procaine penicillin. Aureomycin (AMPOTO & FINDLAY 1950a) and chloramphenicol (AMPOTO & FINDLAY 1950b) by mouth, have been found effective in treating secondary lesions. LOUGHLIN & JOSEPH (1951) report that terramycin (2 g daily by mouth for 5 days) rapidly heals secondary and tertiary yaws lesions. Following the use of penicillin or these other antibiotics secondary lesions cease to be infective in a few days but after none of the more recent antibiotics has adequate serological observation been reported.

The results of treatment of tertiary yaws are less known. Lesions usually respond less rapidly negative serological results require larger doses and are not so readily obtained. Clinical relapses occur Potassium iodide is of value in tertiary yaws

Lesions of the palms soles and bones respond in the same manner as the characteristic skin lesions in the respective stages

There is no occasion for local applications to skin lesions except for protective dressings in tertiary ones Attention to the general condition of the patient *e g* eradication of other infections, improvement of nutrition, etc have more application to individual cases as does serological control than to mass treatment but in long term planning they would not be neglected.

PROGNOSIS

Primary and secondary yaws in otherwise healthy children and young adults is probably a painful and unpleasant disease. When considered as another general infection added to malaria, nutritional deficiencies, *ancylostomiasis and other conditions it may contribute to mortality* Secondary typical yaws on palms and soles may be important in spreading infection especially when they occur more or less alone as relapses.



273 Extensive tertiary yaws ulceration of the face

These and other palm and sole lesions may interfere with work by the pain the use of hands and feet may cause

Severe and extensive tertiary lesions may predispose to terminal infections

VAN NITSEN (1944) considers that, in some parts of the tropics, yaws is responsible for more misery and suffering than all other diseases together and that it is one of the greatest scourges of the indigenous population. GUIMARÃES (1950b) also stresses the serious nature of yaws to a community and adds that if one takes into account the cost

and ineffectiveness of long-continued past efforts to control the disease, the cost of modern antibiotics should not be a deterent to this use.

VAN NITSEN (1944) also reports that the eradication of yaws by mass treatment has not been followed by a great increase in syphilis in the Congo. He points out that other factors than immunity may cause races highly infected with yaws to remain free from syphilis.



274. Same patient as in Fig. 273 after healing.

PREVENTION

Education in the means of spread and prevention of the disease and improved standards of hygiene in a community would almost certainly eradicate yaws from a population in less than a generation, if such measures were possible. HARDING (1949) says there are four possible aims in anti-yaws campaigns: (1) total eradication of yaws; (2) elimination of infectious lesions so that transmission ceases; (3) reduction of yaws to a point at which it does not cause any serious degree of suffering or loss of efficiency in the community in which most of the manifestations are mild and non-infectious; (4) alleviation of symptoms



275 Gangosa with destruction of the nose in tertiary yaws.



276. Advanced but inactive gangosa in tertiary yaws.

by treating cases voluntarily seeking treatment. Although eradication may now be nearer a possibility than when he did his work, his recommendation that the third purpose, to reduce yaws to a low incidence level, is probably still sound for Africa. To achieve this he planned his campaign in Sierra Leone in three stages The first was mass diagnosis and treatment by mobile teams followed immediately by the provision of permanent treatment centres so sited that no inhabitant of the area had more than 10 miles to walk for treatment



277 Goundou in secondary yaws.

and finally home visits by a yaws attendant to detect relapses and new cases in their villages and send them to the clinic for treatment. Unless an adequate follow-up service is instituted it is almost certain that in a few years infections from relapsed secondary lesions will undo all the good achieved by mass treatment This was observed by LAMBERT (1935) in Western Samoa In many parts of the tropics anti yaws campaigns which have fallen far short of their planner s intentions have in a few years resulted in the at least temporary virtual disappearance of secondary cases

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PINTA OR CARATE

V PARDO CASTELLO – Havana
CARLOS CASTANEDO – Havana

DEFINITION

Pinta[1] is an infectious disease, produced by Treponema carateum (BRUMPT), or T herrejoni[2] and characterized by cutaneous lesions with typical and marked changes of colour Synonyms are *mal del pinto blue disease of the Chillos valley Piquite Tiña Cute Catiro Quirique* and *Purú-purú.* The term "*lota*" (Guiana) mentioned by BRUMPT means tinea versicolor What is meant by *guasarola* (Haiti) is not clear

EPIDEMIOLOGY

Pinta is almost exclusively confined to the warm zones of the Americas, and to the coloured races living in these zones. It is predominant among the Indians of the lowlands of Mexico mainly the basin of the river Balsas, and in the valley of Chillos in Colombia. In Cuba pinta was first reported by V PARDO CASTELLO in the year 1930, and a small group of cases has been identified since then, most of them in Negro patients.

In Colombia over 600 000 cases and in Mexico more than 300 000 cases have been reported, almost all in Indians although a low percentage of cases occur in pure white persons. Most of the cases are

[1] The name originates from "pintare" meaning painting
[2] HERREJÓN (Mexico) first advanced the treponemal aetiology BRUMPT described the treponema as T carateum

found in villages and in outskirts of small towns in the lowlands. It is rarely that cases are found at a high altitude and some investigators believe that the disease is transmitted by an insect vector.

RUIZ SANDOVAL (Mexico 1879) believed that it is transmitted by culicoides. MONTOYA Y FLORES and HERREJÓN suspected simulides, mosquitoes or bedbugs as BRUMPT and MAZOTTI did ornithodores.

Treponema carateum has been found in Simulium haematopotum after biting a patient, according to LATAPÍ and the disease has been experimentally inoculated by using a hippelates, but it has not been proved that they are usual vectors.

Probably the disease is transmitted in most cases by direct contact



278. Treponema carateum in the lymph of a pinta-spot.

from one person to another although there is some contradiction in the fact that the disease is limited to special areas. VARELA and AVILA found 56 of children of "pinta parents" suffering from the disease.

ALLAN and GOODALE have described a pinta like condition in Guam (Pacific) called *Paladang*. According to SIMONS the tinea albigena (or khi huen) of South East Asia is not a fungous disease but probably pinta. He described the first case in the Guianas.

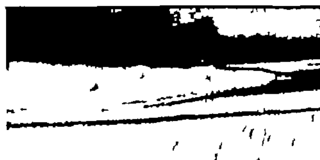
AETIOLOGY

In 1938 GRAU and ALFONSO found the treponema in the lymph of the

lesions of a case of pinta in Cuba. Later studies by LEÓN BLANCO in Mexico demonstrated the presence of this same agent in all untreated Mexican cases. BRUMPT described the morphology of the treponema under the name of Treponema carateum. LEÓN BLANCO later suggested the name T. herrejoni.

The Treponema carateum is morphologically identical with those of syphilis and yaws. It is constantly found in the lymph obtained from the superficial lymph nodes and from lesions of all untreated cases of pinta, as well as in stained sections of the same lesions. To say that ²/₃ of the cases of pinta have no demonstrable treponema (BRUMPT) is a misstatement.

The Treponema carateum is a mobile spiral-like micro-organism with



279 Method of obtaining serum for dark-field examination of pinta. *(F. sal-San Francisco)*

rather close convolutions, numbering 10 to 15, and its size is from 7 to 20 microns. The ends are pointed and no flagella have been demonstrated.

It has been successfully inoculated experimentally into human beings, producing typical clinical lesions of pinta, (TELLEZ, LEÓN BLANCO) and also inoculated into the scrotum of rabbits producing typical lesions. According to LEÓN BLANCO the treponema may also be found in the sweat of some patients. The *incubation period* varies between one and three weeks.

SYMPTOMATOLOGY

Three successive stages of development can be described in pinta.

1st stage —Initial lesion —Since the initial lesion of pinta is not readily apparent to the patient, it is rare to see one spontaneously acquired. We owe our knowledge of it mainly to inoculation for experimental studies. The *incubation period* varies from one to three weeks The initial lesion may be single or multiple and in non experimental cases it is usually located in the uncovered areas, particularly the lower limbs

Initially there is a small papule, appearing two or three weeks after inoculation, which slowly develops in size and depth and becomes



280 Primary lesion of pinta.

covered with scales but never ulcerates There are no subjective symptoms and no secondary adenitis

This papule grows, by peripheral extension, into an erythemato-squamous patch with sharply defined borders covered with scales and usually shows bizarre and characteristic dyschromias consisting mainly of different shades of red and brown.

2nd stage —Pintids —After two to six months of development of the initial manifestations disseminated lesions begin to appear in different regions of the body These lesions resemble the mother lesion from the first stage and develop along similar lines.

In the second stage there may be only a few lesions or many

appearing successively and these gradually become dyschromic, thus giving a peculiar and characteristic picture.

The initial lesion does not disappear but continues its evolution, and becomes indistinguishable from the others. All these lesions have been named *pintids*" by LATAPÍ and LEÓN BLANCO and ascribed to a haematogenous dissemination of the disease.

The eruption consists of one to scores of individual lesions, with sharply defined borders, distributed mainly in the lower limbs although they may appear in any part of the body The unilateral form is also called *hemi-pinta*

Pintids do not show any tendency to symmetry and are vari-



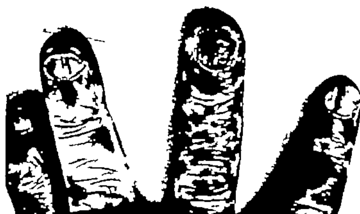
281 Characteristical triangular leukoderma in pinta. Note rest of pigment in the leukoderm.

coloured and bizarre, usually with policyclic borders. Some are erythemato-squamous patches others whitish and hyperkeratotic, others achromic and other slate blue, and in some cases bluish-black (*carate plombé*) Yet some may resemble such erythemato-squamous lesions of the skin as tinea circinata, eczema and psoriasis.

These lesions are not itchy and grow slowly for years and usually end up as purely dyschromic lesions which are considered late mani festations. Pruritus usually indicates uncleanliness or secondary infection.

During the "pintid" stage, there is a definite enlargement of the lymph nodes and the blood cell count often shows basophilia and eosinophilia. There are no subjective symptoms.

3rd stage —Late Manifestations —There is no sharp line of demarcation between pintids and late manifestations of pinta the pintids grow for some years and then some of them disappear altogether while others evolve to the stage of late manifestations at this time, more lesions appear which are of the type of late manifestations from the very beginning



282. Pinta from Brazil
(Orig G Castro-Belo Horizonte)

This period has been called "dyschromic" for although dyschromias are the rule in all lesions of pinta it is in this stage that they become more prominent while the squamous character of the pintids becomes less and less noticeable

Also while pintids are asymmetric, late manifestations tend to symmetry and to generalization The extensor aspects of the limbs are the sites of predilection, as also the face hands and feet The genitals and the folds of the skin are usually free of lesions. The patches of colour become well defined in the third stage, and therefore three types are common in Mexico *i.e.* red, white and blue pinta, which have been so named according to the types of predominant lesions

although all three types may be present in the same individual. (See p 181)

In Cuba the late manifestations consist of patches of hyperpigmentation and achromia, mainly of the hands and feet, usually accompanied by palmoplantar hyperkeratoses and some atrophy of the skin. The Mexican authors have reported vitiligo-like lesions in very old cases (*carate muerto* or burnt out pinta) and GUIMARAES and other have described *pintoid yaws* Some cases of yaws may indeed show lesions of discoloration similar to those of pinta. The condition of distal



283. Pinta of the foot.

(Nery Guimaraes Rio de Janeiro)

discolouration of the extremities may also occasionally appear as the result of syphilis. The differential diagnosis of these cases must rest on the history of the patient, on animal inoculations and on a study of the pathological changes. Treponemata of pinta, syphilis and yaws are indistinguishable. In yaws and syphilis the discoloured lesions are late manifestations, and may appear many years after contracting the disease[1] It has not been proved that pinta can cause abortion and the

[1] *Cutaneous achromia*, a sequel of many skin diseases, should not be confused with pinta when it complicates syphilis or yaws. See chapters 1 4 5 and 7).

cardio-vascular and CNS lesions observed in occasional cases have not been proved to be due to the treponema of pinta

Atrophy of the skin is constant in old cases, and also alopecia of the affected parts. Some onychodystrophies have been reported.

Pigmentation of the mucous membranes has been observed in pinta,



284 Pinta of the sole of the f ot.

but it is not frequent furthermore, similar pigmentation is a normal occurrence in the col oured races and cannot be identified with pinta.

Onychia may be observed in cases of pinta affecting the extremities of the fingers it is usually squamous and pigmented It is mentioned in this paper Dermatographism cannot possibly have any connection

with pinta since it is a neurovascular phenomenon usually occurring in allergic conditions.

There is some disagreement as to whether late pinta can produce internal changes. The Mexican authors do not believe there are any but in Cuba some cases showed evidence of aortitis, and others had pathological changes of the spinal fluid. Further studies may solve



285 Histology of pinta.
(Fasal–San Francisco)

this interesting question. BRUMPT according to his book, may have seen gangosa occurring in pinta, but we have never seen it.

"Pinta" in cattle is unknown to us and we have no notion of the influence of food in the production of pinta either in animals or in man.

PATHOLOGY

The histopathology of the early lesions of pinta has been studied mainly by LEÓN BLANCO. In the initial lesion the epidermis may be slightly thickened and oedematous and the papillae are elongated.

There is an intercellular infiltration of lymphocytes. Pigment is scarce in the basal layer. In the dermis there is a thick infiltrate of lymphocytes and plasma cells with occasional histiocytes and polynuclears. The papillary layer is abundant in chromatophores. The distribution of this infiltrate tends to follow that of the blood vessels. It is striking that even at this early stage the distribution of pigment is already altered.

The histopathology of the pintids varies with the clinical type, but the fundamental changes are the same in all of them. There is hyper



286 Pigmentation of the mucous membranes has been observed in Pinta, but is not frequent. One should bear in mind that pigmentation of the oral mucosa is quite common in the coloured races.

(Nery Guimaraes: Rio de Janeiro)

keratosis and parakeratosis and some acanthosis and sometimes there are microabscesses. Pigment is almost absent from the basal layer. In the dermis one finds a dense inflammatory infiltrate especially around blood vessels with the same cellular types as in the initial lesions. Melanophores are abundant in the papillary and subpapillary layers.

The late lesions are the best known and have been studied by OCHOTORENA, PALLARÉS, LEÓN BLANCO and others. The changes consist of atrophy of the epidermis, absence of pigment in the basal layer, great quantities of melanophores in the upper dermis and a continuous

band like lymphocytic infiltration of the upper dermis. Very frequently a marked hyperkeratosis can be seen.

Special stains demonstrate treponema in lesions of all the stages They are found in great numbers in the malpighian layer

SEROLOGY

In 1926 and 1927 WALTER MENK and GONZÁLEZ HERREJÓN independently called attention to the fact that almost all cases of pinta had positive Wassermann tests.

Further studies have shown that in the first stage serological reactions are negative. It is well into the pintid stage that blood tests become positive in about 80 % of the cases while 100 % of those with late manifestations give positive reactions.

While serological reversal occurs under treatment in some cases in others it has not been obtained, even though the patient has remained clinically well.

IMMUNOLOGY

Since the discovery of the causal agent of pinta, many experiments have been performed to establish it as a clinical entity different from other treponematoses, and to determine whether it may produce immunity

By experimental inoculations in men the following facts have been established

1 Pinta can be inoculated in a healthy individual by depositing lymph from a pinta lesion on an abrasion of the skin.
2 Pinta can be successfully inoculated in syphilitics.
3 Cured cases of pinta show relative immunity developing atypical initial lesions, but no pintids or late manifestations.
4 Pinta in its late stages confers immunity against reinfection.
5 Mexican "mal del pinto" and Cuban "pinta" are the same disease.

DIAGNOSIS

The typical case of pinta presents a strikingly characteristic clinical picture, which is difficult to confuse with any other disease. However late cases must be distinguished from vitiligo with its dark borders

and its predilection for the orifices and some of the early ones from chronic eczema, tinea circinata, psoriasis and leprosy

Albinism is a congenital condition, often familial and therefore seen in several members of the same family often with the same pattern when it is partial and not universal. Leopard skin [1] is a term applied to some cases of vitiligo with increased pigmention of the unaffected skin or to some cases of partial albinism. The leukoderma of leprosy



287 Pinta leukoderma persists after arsenical therapy

is analgetic and anhidrotic and the lepromine test will be positive in tuberculoid leprosy The histamin test will show an abnormal reaction (wheal without erythema) in leprosy

The simplest and surest way to make this differentiation is by taking

[1] The name of spotted wood skin in Surinam originates from the South American wood brosimum discolor" from the piratinera guianensis tree The Indians make their bows from a non-potted kind of this wood. (Simons)

a specimen of lymph from one of the lesions and examining it for treponemas under the dark field microscope. Pinta lesions are teeming with these organisms.

In some treated cases it will be necessary to resort to serological



288. Pintoid yaws is the term given to the quartet yaws, hyperkeratosis palmoplantaris, achromia and juxta-articular nodes.

(Nery Guimaraes–Rio de Janeiro)

reactions and to stained sections. In seronegative achromias we should beware of diagnosing pinta.

The difficulty of diagnosing pinta from syphilis in some cases is almost unsurmountable, unless one is able to perform experimental inoculations

THERAPY

Pinta lesions disappear easily with specific treatment as used for syphilis and yaws. Penicillin, neoarsphenamine, mapharsen, and bismuth, are able to cure most of the skin lesions completely with a return to normal. In late lesions usually the hyperpigmentation is almost totally eliminated, but the achromic areas remain. The hyperkeratosis is cured in all lesions.

The serological reactions become negative in some cases but in Cuban cases studied by V. PARDO CASTELLÓ no amount of treatment succeeded in bringing about serological reversal.

Penicillin is the drug of election, being less toxic than arsenic and bismuth, and at least as effective. Probably as in other treponematoses, the crystalline-G fraction of sodium penicillin is the most active against pinta; we believe that 4 000 000 Oxford units of crystalline-G sodium penicillin should be an adequate treatment.

Recently it has been shown that as little as 1,200 000 units of procain penicillin-G with 2 % aluminium monostearate in one dose (oily) may be sufficient to clear up a case of pinta. This greatly facilitates the treatment of large numbers of people as in Mexico and Colombia.

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CHAPTER 9

GOUNDOU

P BOTREAU-ROUSSEL

Marseilles

DEFINITION

Goundou is a hypertrophic osteitis of the facial bones, in particular of the nasal bones and of the ascending frontal process of the superior maxilla. In most cases symmetrical more or less large bony exostoses are formed on either side of the nose The cause of this hypertrophic osteitis has long been misunderstood but the disease is a sequel to yaws and does not show any clinical or histological difference from other forms of yaws-osteitis which appear more frequently on the long bones and on the bones of the hand. Goundou is the most exceptional localization of all forms of yaws-osteitis the number of cases amounting to scarcely 1 °/₀₀ of the total number of these osteites, even in countries where it is most frequently found.

HISTORY

MACALISTER (1882) and LAMPREY (1887) reported "the existence of horned men in Africa" In 1894 STRACHAN reported 3 cases of bony overgrowth or exostosis in the West Indian Negro" in Jamaica but it was MACLAUD who in 1895 called attention to the syndrome and gave it the name of goundou or "anakhré" [1] by which names the disease has since been known.

[1] *N'Goundou* in Agni dialect and N'*[illegible]* in Attie dialect (eastern part of the Ivory Coast) have the same signification both terms mean "big nose" or "enlargement of the nose

MACLAUD's description—which, for that matter was incorrect—has often been reproduced in the literature, and may be summed up as follows. The disease first appears during late childhood more rarely during adolescence It starts with an intranasal inflammation characterized by violent headache and a purulent discharge from the nose. Some thickening of the ascending frontal processes of the superior maxilla precedes the appearance of the swellings, which, at first, are quite small, hardly the size of a pea. The headache gradually lessens the discharge stops, but the hyperostoses continue to grow When the patient is about 15 they are the size of an almond at 20 as large as a pigeon's egg at 30, a hen's egg, later on, the goundou may be as large as a fist, etc... The two tumours are symmetrical and situated



289 Goundou in 10 years old girl, having acquired yaws at the age of three. Arrested since one year The sight is almost lost.

on either side of the nose along the direction of the ascending process of the *superior maxilla* They are painless of an osseous consistency do not affect either the skin or the mucous membranes and never suppurate. The only complication is a progressive restriction of the patient's field of vision, which may finally lead to almost complete blindness owing to the mechanical obstruction of the patient's eye sight.

In 1900 CHALMERS published 5 cases of goundou observed on the Gold Coast, in a district quite close to the Agni country This author has doubtless seen many more cases in several of which he operated. He reported that these tumours may suddenly stop growing, and that in certain cases there is a tumour on one side only Finally CHALMERS

was the first to attribute goundou to yaws, but he did not insist on this point in the successive editions of the treatise which he published on the subject, in collaboration with CASTELLANI

Since MACLAUD and CHALMERS numerous cases of goundou have been reported the majority from Africa, but also from other tropical countries (Antilles, Brazil, Venezuela, Mexico South China, Ceylon, Malay Peninsula, Java, Sumatra, Oceania) while many authors reported cases accompanied by lesions of the long bones. Other authors have also described lesions of the long bones as a sequel of yaws.

In 1916 the present writer observed 121 cases on the Ivory Coast, of which he operated on 113 The majority of these patients had lesions of the long bones as well as of the facial bones During 1934—1936 his co-workers also operated more than 100 cases [1]

The geographical range of goundou, therefore, covers the whole of the intertropical zone and mixes with the geographical area of yaws

AETIOLOGY PATHOGENESIS and EPIDEMIOLOGY

Neither age, sex, nor race plays any part in the development of this syndrome, the only important factors being those which contribute to the greater or lesser virulence of yaws *i.e.* the total absence of the most elementary hygiene and the complete lack of any form of treatment

The theory put forward by LAMPREY of an anatomical disposition specific to the black races has now been completely abandoned.

Following MACLAUD the hypothesis of an intranasal infection has often been adduced CHALMERS, too, while attributing goundou to yaws still believed that intranasal yaws was necessary for it to occur *FRIEDRICHSEN—a unicist who identifies yaws with syphilis—*also holds the cause to be infection by the nails of an intranasal lesion

Intranasal infection, however could not explain the osteites of the frontomalar bones and of the inferior maxilla

Neither do we support the hypothesis ascribing goundou to syphilis

[1] All these patients were attracted by the aesthetic benefit derived from the operation, which rid them of this horrible infirmity During the years 1917 1934 when my successors were taking no interest in the surgical treatment of goundou not a single case was reported on the Ivory Coast because the patients in their shame had gone into hiding again

those who like FRIEDRICHSEN hold this view are unicists and confuse yaws with syphilis. On the contrary we have always found yaws among our patients antecedents and while, in 1917 we already had occasion to watch goundou develop in a young yaws patient, during 1934–1936 we observed the appearance and development of goundou during the secondary eruption of yaws in no fewer than 32 cases



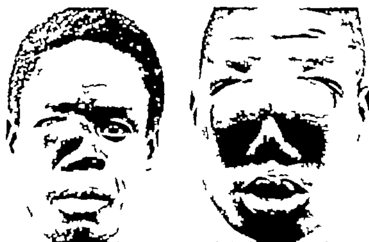
200 Goundou and yaws. Note lower legs—tibia thickened.

These findings have since been confirmed by a large number of investigators of whom I shall only cite CLAPIER in equatorial Africa and HACKETT during his yaws-research mission in Uganda.

None the less, many authors put forward the frequency of goundou on the west coast of Africa, particularly on the banks of the Bight of

Benin, as compared with its rarity in southern Asia, as an argument against goundou being due to yaws [1]

One cannot, however reasonably compare the civilization of the population of southern Asia with that of the Ivory Coast, which, in 1912, still lived, so to speak, in the stone age. Entire tribes crammed together in the sectors covered by dense tropical forests were unaware of the existence of salt or sugar and used the ashes of certain plants as condiments for their food. Woe betide the imprudent neighbour who lost his way into their territory he was at once cut to pieces and devoured. Sickness, to these people was either a punishment due to



291 Unilateral and bilateral goundou.

the wrath of their gods, or caused by some wizard, and they were completely ignorant of every form of therapy even the very simplest

[1] I started as medical officer of health in Indo-China (1907 1911) and continued in the same capacity on the Ivory Coast from 1912 until 1917 It so happened that I went back to the Ivory Coast as Director of the Health Service (1934 1936), and to Indo-China as Inspector-General of Hygiene and Public Health (1941 1945). While during the former two sojourns my activities were limited to my medical post, during the latter two my functions obliged me to make frequent tours of inspection which gave me a chance to visit every region on the Ivory Coast and in Indo-China. I am therefore in a position to compare with first hand knowledge the prevalence of yaws in southern Asia with that on the banks of the Bight of Benin.

Indeed, the entire population, without exception, pays tribute to yaws in every village, at any time, one finds children in full eruption. It is not surprising, therefore that yaws of such virulence is not found anywhere else. On the Ivory Coast itself yaws is becoming less frequent and less virulent according as one leaves the forest and approaches the desert and the disease is actually rare in the open, cultivated parts of the Sudan, where practically no more osteitis or goundou is found today

In Indo-China, on the other hand, yaws is relatively rare and localized at certain points, *i.e.* the Coast of Annam the forest region of Cambodia the forest region of Laos, and a group of 5 or 6 villages



292. Goundou of the maxilla and frontal mandibula.



292a. Goundou of the zygoma.

in Tongking and—a most important fact—the disease has always been treated, even before the arrival of the Europeans. The Sino-Annamite pharmacopoeia makes ample use of both mercury and iodine which, until about 50 years ago, were our only weapons in the fight against yaws Its virulence in these regions, therefore, has become greatly attenuated. Nevertheless, I have found—although far more rarely—every form of bony lesions observed in West Africa, including *two cases of goundou*[1] *(Goundou in Asia* has been described by Brandon Maxwell, Lim Boon Keng, Wick, and others.)

[1] Unfortunately the whole of my documentation concerning the bony lesions caused by yaws in Indo-China, including photographs, radiograms and notes was destroyed at Hanoi in 1945 during the disturbances following the Japanese occupation.

SYMPTOMATOLOGY

Let me state at once that yaws, when left alone, nearly always becomes "arrested" of its own accord, and that the natural defences of the organism usually succeed in defeating the spirochaetes sometimes after a relatively short time, in other cases more slowly and varying greatly as between one patient and another But this arrest does not imply the disappearance of all the sequels To confine ourselves to the one that interests us here, goundou, the bony swellings will remain at the stage of development at which they were when the patient recovered from his yaws, although this is not really quite correct they do undergo a



293 Goundou of the maxilla.

very slight diminution owing to the disappearance of the inflamed tissue and the consequent formation of the bony tissue.

The goundou tumours usually appear in the course of the yaws, simultaneously with the other bony lesions in some cases as early as the first weeks of the disease[1] but most often when the disease has already developed for several months sometimes immediately after the eruption has disappeared, and in rare cases not until several years

[1] When writing my first publications on goundou and yaws osteites (1917) I considered them to be tertiary lesions. Actually they are secondary lesions which often appear almost simultaneously with the eruption. They are never ulcerous or necrotic, as for instance gangosa and the tertiary lesions of the long bones so thoroughly studied and well described by HACKETT

after The appearance of the swellings is always coupled with fairly sharp pains of the type of frontal headache, the pains being more violent according as the time that elapsed between their appearance and the onset of yaws was shorter

At first the swellings are tumefactions rather than genuine tumours, and they are even more noticeable to the eye than to the touch, palpation giving one the impression that they have the consistency of inflammatory rather than bony tissue. These tumefactions are frequent very often they disappear spontaneously without leaving any trace, providing recovery from yaws follows quickly enough—in other words, they invariably disappear when the yaws is treated in good time.

If the disease is left alone the course of its progress varies extremely as between one patient and another In some cases the yaws is not highly virulent the facial osteites develops fairly slowly ending up after about 4—5 years as small, very hard bony tumours the size of a pea, a bean, an almond or a nut, after which they alter no more either in shape or in volume. They may appear on one side only the so-called "*unilateral goundou*"

In other cases on the contrary when the yaws is highly virulent, the tumours grow very rapidly sometimes, even in young children, to the size of a hen's egg a billiard ball or even as large as a fist, and very soon obstructing more or less completely the patient's field of vision before recovery from the yaws can stop the progress of this hypertrophic osteitis.

More rarely the osteitis does not remain localized in the ascending processes of the superior maxilla, but extends to another part, or even to the whole of that bone

As is the case with para-nasal tumours, this swelling may only be slight, and be arrested fairly quickly leaving no other sequelae than a certain enlargement of the face and, perhaps, a slight widening of the distance between the upper incisors. If on the other hand the yaws is highly virulent and the disease progresses rapidly it may in very rare cases end in the most monstrous deformations. When only the anterior part of the maxilla, which is in front of the dental arch, is affected, a kind of snout is formed which draws a more or less deformed nose along with it. When the entire bone is affected,

a monstrous tumour develops of which I once saw an example the size of a foetal head (Fig. 293). The molars remain in their normal place, but the premolars, the canines and the incisors assume a somewhat haphazard alignment, unless they are summarily expelled by the osteitic process.

Again, goundou is not always localized in the superior maxilla. In one case it was strictly limited to the nasal bone proper; the tumour was the size of a chick pea and the nasomaxillary suture was only slightly enlarged to support this tiny hypertrophic bone. The malar, frontal and parietal bones and the inferior maxilla at the level



294. Spring in goundou

of the chin may be affected either individually or simultaneously with the superior maxilla, and, in common with the latter, may either recover rapidly or continue to swell for years on end according to the virulence of the yaws (Fig. 292).

ANATOMY AND HISTOLOGY

Macroscopically, the texture of these tumours is not the same while they are in full development as when their growth has been arrested.

When the young tumour is growing rapidly under a still healthy skin, an inflammatory and considerably thickened periosteum is found, which can only with difficulty be detached from the bone. There is no *plan de clivage*; the periosteum cannot be separated from the cortex of

the bone, into which the raspatory readily penetrates The bone is tender the haversian canals are much dilated and filled with inflammatory yellow marrow The lancet easily incises this bone, which can be cut about at will this facilitates the surgeon s work when he is dealing with voluminous growths

When, on the other hand, the tumours are small, their growth having been arrested long since, one finds a thin periosteum which quite readily detaches itself from the very hard bone. The bone is difficult to tackle with the chisel a tap of the instrument may fracture it. Its texture resembles that of ivory In certain rare cases these old



295 Skull with goundou in Dupuytren Museum, Paris.

tumours show a structural system ("système de cloisonnement") and cells comparable to those of the mastoid and in one case the maxillary sinus had pushed a prolongation into the interior of a stabilized paranasal tumour

Between these two extremes all kinds of intermediate forms are found, according to the developmental stage of the affection.

Microscopically goundou tumours have been studied by CORNIL and GAUTHIERS VILLARS. Only tumours in course of development are interesting to the histologist old tumours are very hard to cut and no longer show any specific feature

The description given by these authors is too important to reproduce

here and should be read in the articles specially dealing with this tudy Here follows a brief summary of the essential parts

Osteites of the a cending process of the superior maxilla may perfectly well be regarded as based on old osteitis of the long bones due to yaws This is not surpri ing since all the material examined was from operations in relatively old cases of osteiti while no biopsies were made of very young gound ous at the time of their initial appearance since all these cases were succes fully treated medically

The enlargement of the perio teum may be regarded as identical



FIG 79 Diffuse goundou of the ma illa pontaneou ly arrested within 30 rs The ight hand phot graph taken 18 y rs later

with the lamellar periosteal hyperplasia in syphilitic osteitis The second interesting fact is the hypertrophy of the pongioid tissue in which the trabeculae are more numerous and larger than is normally seen while certain details strongly suggest the proliferative neoformati n of these trabeculae In the modifications caused in the structure t the pongioid areolae two facts predominate on the one hand, the collagenic sclerosis which is fibrillary and irregularly distributed especially in the vicinity of osseous trabeculae sometimes numerou fibropla tic formations while there is a constant ab ence of adipose cells and osteoblasts On the other hand there are cellular congl merations in the perivascular regions consisting for

the most part of plasmocytes, which facilitates our approach to this type of lesion, which has been described under the name of "syphilitic plasmoma" We are well aware that there are quite a number



298–300 Goundou of the maxilla one month and 18 years after surgical treatment.

of common inflammations which may give rise to plasmoid formations that could never be regarded as syphilitic but we do believe that there is every reason to attribute the character of one might say treponematic specificity to the bone marrow in these cases of inflammatory formations"

RADIOGRAPHY

Radiography only confirms what we have learned from our clinical and pathological investigations.

Young goundous, still susceptible to rapid cure by medical treatment, let the roentgen rays pass through them, since they are not yet calcified. A little later there is already some bone. The inflammatory tissues disappear under the influence of medical treatment, but the bone remains.

Finally, in old goundou tumours there is only hard compact bone.

In voluminous goundous that have developed rapidly, one dis-



301. Excellent result of surgical therapy of rapid growing goundou. The right hand photograph was taken 18 years later.

tinctly sees the dilatations of the intratrabecular spaces, which give to the radiogram an aspect like that of a coralliferous polypus attached to its rock (Fig. 294).

PROGNOSIS

Apart from the obstruction of the field of vision, which may occur in certain rapidly developing cases, the prognosis of *goundou* presents no grave contingencies. The disease is a pathological curiosity which is bound to disappear with the progress of health and public hygiene in the tropical zone. Yaws is nowadays being treated everywhere, and if it does not disappear completely, it will at

any rate become extremely rare, as it already is in the Antilles and in Brazil. In any event, the disease will soon lose the really extraordinary virulence which it shows on the banks of the Bight of Benin.

The populations of the Ivory Coast and the Gold Coast were swept, as it were, from the stone age to modern times during the past half century They may not yet have assimilated our civilization but they are already benefiting from modern scientific progress, brought and applied by European scientists. It may safely be affirmed that goundou, rare as it already is, will in future be known to our successors only from the illustrations and descriptions in our treatises.

THERAPY

The treatment of goundou in its early stages is purely medical, and closely resembles that of yaws. Bismuth compounds take first place in the therapy The tumours, when treated in good time, will disappear entirely At a later stage the treatment can only be palliative it will arrest the osteitic process, but it has no effect on already formed bone.

Fortunately surgical treatment produces results of an aesthetic nature which are greatly appreciated and keenly sought by even the most primitive natives.

In my operations during 1916 and 1917 I used chloroform anaesthesia. Later (1934—1936) all operations were performed under local anaesthetic (novocaine 1 200) Only the tissues are sensitive to pain the bone itself may be painlessly resected.

In the case of large tumours in full course of development, it is necessary for satisfactory aesthetic result, to cut away the redundant skin and to excise the periosteum In old tumours on the other hand, the operation is quite simple and consists, after incision and rapid removal of the periosteum, in splitting up the tumour by striking it with the chisel.

In very voluminous, still growing tumours, where inflammatory tissue predominates and one is obliged, as it were, to "sculpt" a human face out of this mass it is advisable (I did not do this in 1917) to give the patient medical treatment for three months before the operation, as otherwise the sudden cure of the hypertrophic process may later on, be followed by a considerable regression of the face, thus spoiling the aesthetic result

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CHAPTER 10

RAT BITE FEVER

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Rat-bite fever is a widely distributed sporadic infection transmitted by the bites of rats or other animals. In man it is characterized by a lesion at the site of the bite, fever of a relapsing type, and a rash. The condition may be caused by a spirillum or a streptobacillus, and the two forms are known as *sodoku* and *Haverhill fever* respectively.

SODOKU

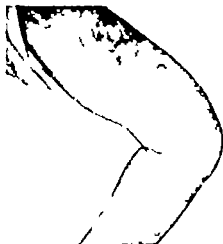
AETIOLOGY AND EPIDEMIOLOGY

The causal organism, *Spirillum minus* is a short rigid spiral organism, very actively motile by means of terminal flagella. It is a natural parasite of rats and certain other rodents, but cats, ferrets and dogs have also been found infected. The spirilla are not normally found in the saliva except when the rats have lesions in the respiratory tract, and it is thought that the organisms reach the mouth through lacerations of the mucous membrane incurred when biting. Spirilla have been demonstrated lying immediately below the sarcolemma of the muscle fibres of the tongue, from which they could escape if the thin covering layer of epithelium were ruptured.

SYMPTOMATOLOGY

At the time of the bite, the surrounding area and the regional lymph glands may become inflamed, but the lesion generally heals in a few days provided that no secondary septic infection occurs. The *incubation*

period of sodoku varies from 5—30 days but is most commonly about 2 weeks. The onset of symptoms is generally sudden, with fever of 39—40 C, headache, pains in the muscles and joints, nausea, and severe prostration. The original skin lesion now becomes inflamed and oede



301. The local lesion twenty days after the bite. Showing the brawny induration and exudation. S. minus isolated from this lesion.
(Indian Medical Gazette)



302. Patient bitten one month previously. The local lesion on the left shoulder was cauterised with nitric acid and an ulcer has formed covered by a black slough. The rash is well seen on the left arm.
(Indian Medical Gazette)

matous vesicles appear and may become necrotic an irregularly shaped ulcer with raised, oedematous edges develops, its base covered with granulation tissue (Fig 302)

A skin rash may also accompany the fever (Fig 302a) The eruption is maculo-papular in type, and of a purplish-red colour it is distributed irregularly over the body The spots, which are very variable in size, are generally discrete, but may tend to coalesce on the patient s back. Patches of *urticaria* may also occur

A leucocytosis is present during the pyrexial attacks, but subsides during the afebrile periods. The eosinophiles may be increased in number and the lymphocytes decreased. The Wassermann and Kahn tests may give positive reactions. In untreated cases an increasing degree of secondary anaemia develops.

The initial febrile attack lasts for 3 or 4 days, and then the temperature falls by crisis, the rash often disappearing at the same time. After an apyrexial period, of variable length but generally from 6 to 10 days, there is a febrile relapse, which is usually less severe and of shorter duration than the primary attack, and which is less often accompanied by the rash. In untreated cases relapses may continue for weeks or months, becoming milder as time goes on, and finally ceasing spontaneously as immunity is established and the infection overcome.

In untreated cases the mortality may reach 10° but, with modern chemotherapy rapid and complete recovery is the rule, and the death-rate is negligible

DIAGNOSIS

The symptoms and the course of infection, coupled with a history of being bitten by a rat, are often sufficient to establish the diagnosis. Full confirmation can be obtained by demonstrating the presence of the spirillum, preferably by the inoculation of white mice with 0.5 ml of venous blood taken during a febrile period. From the 8th day onwards after inoculation mouse blood should be examined by dark field microscopy The great activity of the spirilla makes it easy to differentiate them from the blood filaments and other artefacts which often cause difficulty in these examinations. Fluid obtained from the oedematous area around the bite can be examined in the same way

or used to make smears to be stained by GIEMSA's or FONTANA's stains but these methods often fail to demonstrate the parasites.

The conditions with which sodoku is most likely to be confused are filariasis, especially filarial lymphangitis, relapsing fever and dengue. The temperature charts and the presence of microfilariae or treponemes in the blood in these diseases will serve to distinguish sodoku from them, but the differentiation between it and the other form of rat bite fever caused by *Streptobacillus moniliformis* can be made with certainty only by the isolation of the causal organisms (See Haverhill Fever).

THERAPY

Arsenical drugs have a specific curative effect and, before the introduction of antibiotics, the usual treatment was 3—6 injections of 0.4 to 0.6 g. of neoarsphenamine. Within recent years penicillin and streptomycin have been shown to be effective and in the future they may supercede the arsenicals.

PREVENTION

This entails the anti-rodent measures which are used for other diseases transmitted by rats. In the event of being bitten, the site should be immediately cauterized.

HAVERHILL FEVER

AETIOLOGY

The other variety of rat bite fever is due to infection with *Streptobacillus moniliformis*, a Gram-negative facultatively anaerobic organism, probably identical with *Actinomyces muris*. For growth in artificial media it requires a high concentration (20—30 per cent.) of serum, a point of practical importance when attempts are made to isolate it in blood cultures. On LOEFFLER's serum medium the organism develops slender branching filaments, which grow in intertwining masses and often show central, terminal or sub-terminal enlargements (moniliform bodies). In blood-cultures visible growth appears in 18—24 hours, in the shape of small fluffy masses lying just above the layer of sedimented blood-corpuscles. Pleomorphism is marked, and a pleuropneumonia-like organism — the L 1 variant — may develop. Thus

variant has been isolated from human cases after the administration of penicillin, and may represent a resistant form of the organism.

EPIDEMIOLOGY

The streptobacillus is a normal inhabitant of the nasopharynx of rats, from which it may be transmitted directly to man by bites. In other instances, however the disease is contracted by the ingestion of contaminated food, especially raw milk.

SYMPTOMATOLOGY

As a rule the *incubation period* is short, 2—3 days and no ulcer develops at the site of the bite (in rat-bite cases) though the limb may become swollen and painful. The rash is morbilliform or petechial, the fever is of an irregular relapsing type, and arthritis, periostitis, or perichondrit is may be present. During recrudescences, urticarial plaques may appear on the back, legs or buttocks.

DIAGNOSIS

The shorter incubation period, absence of local reaction at the site of the bite, and the presence of arthritis help to distinguish this disease from sodoku, and the diagnosis can be confirmed either by isolating the streptobacillus from the blood, or by demonstrating the presence of specific agglutinins in the patient's serum.

THERAPY

Arsenicals have little curative action, but penicillin is generally effective in treatment. In the cases mentioned above however the antibiotic apparently caused the emergence of the L1 variant, which required an additional course of aureomycin therapy to effect cure.

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CHAPTER 11

CUTANEOUS LEISHMANIASIS

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DEFINITION

Leishmania cutanea – Oriental sore – is a specific granuloma of the skin caused by the flagellate *Leishmania tropica*. It exhibits various clinical forms which will be described below.

HISTORY

BOROVSKY, a military surgeon in Tashkent, published the first description of the parasite in 1898.

In May 1903 LEISHMAN described the protozoon which is the pathologic agent of Kala azar; his description was followed closely by DONOVAN's independent report in July 1903. WRIGHT (1903) found the typical organism of Oriental sore, which was probably already discovered in 1885 by CUNNINGHAM.

EPIDEMIOLOGY

The disease has a wide but not uniform distribution in the old and new world. Cases have been found in Italy, Sicily, Sardinia, Greece (particularly in Crete), Portugal, Spain, the Transcaucasian republics Azerbaidjan, Georgia and Armenia, Asia Minor, Syria, Palestine, Iraq, Persia, Turkey (Central and Eastern Anatolia), India (particularly the North West provinces), Middle Asia (former Turkestan and Bukhara), Afghanistan, the whole African Mediterranean coast (the whole Mediterranean Basin), Abyssinia, Sudan, Eritrea, the French

Congo the Cameroons, French West Africa, Nigeria, Senegal, Tripolitania and Cyrenaica, Panama Canal Zone, Costa Rica.

It must be pointed out that the distribution is not uniform throughout endemic areas. There are centres such as Baghdad where scarcely one person escapes the disease while other centres have relatively few cases. MAYER and NAUK claim that the epidemiology of Leishmania cutanea depends on special climatic conditions a hot and dry summer and short winter. CHATTON and MUEHLENS emphasize that cutaneous leishmaniasis is widespread in regions which have much sand and rocks. Nevertheless coastal areas and river banks are not excluded. (COUSSA)

The greatest part of the endemic foci in the Near East — Iraq Palestine, Persia and Anatolia in Turkey are characterized by a long dry summer and a short winter In Palestine two endemic foci are in the sandy regions having a high salinity of the soil. The oft repeated statement that improvement in road communications helps to spread Oriental boil from endemic foci to new places still lacks confirmation. Apart from sporadic cases which can appear at any place which has a warm climate and where phlebotomus is present, there are constant endemic foci with outbreaks in certain areas following the advent of non-immune arrivals. The disease often occurs in small outbreaks, separated by long intervals of time. Increase in morbidity in endemic districts is often due to particulary favourable conditions for the breeding of sandflies. Such are poor hygienic conditions, cracks in the buildings, caves and dungheaps in the proximity of residential quarters. HOLMES reported numerous cases of oriental sore from Quetta after an earth-quake.

AETIOLOGY

Description of the parasite

In the mammalian host, *Leishmania tropica* is specifically a parasite of the reticulo-endothelial cells, and multiplies in these cells only It is enclosed in vacuoles in the protoplasm of infected cells A varying number of parasites are enclosed in each vacuole. In these cells the parasites assume the form of the so-called Leishman-Donovan bodies. The typical L. D body is an elliptical mass of protoplasm, containing a nucleus and a parabasal body which consists of a small rod-like

mass of chromatin and a minute blepharoplast Occasionally a rhizoplast is seen protruding from the parabasal body but it does not extend beyond the body of the protoplasm In the neighbourhood of the parabasal body there is constantly present a minute eosinophil vacuole whose function is unknown. The L. D bodies are 2–4 μ in diameter

Stained with LEISHMAN'S or WRIGHT'S stain, the protoplasm is



303 L D bodies.

pale blue the nucleus dark the parabasal body still darker

Culture

Leishmania tropica is readily cultivated on a number of media containing rabbit blood or rabbit serum. One of the commonest media is N N N medium (NOVY MCNEAL and NICOLL)

Agar 14 g
Sodium chloride 6 g
Distilled water 900 g

Other media which are also used are NOGUCHI'S semi-solid, leptospiral medium or its modifications. All media used must be

absolutely sterile because *L. tropica* does not long survive in the presence of bacteria. This is a fact of fundamental importance in considering the insect vector. In cultures and in sandflies *L. tropica* assumes a leptomonad flagellate form. On semi-solid media made up with specific immune serum *L. tropica* grows in colonies some of which may be composed entirely of a flagellate form (ADLER) HAWKING has succeeded in cultivating L.D bodies in tissue culture,



304 Phlebotomus papatasii.

employing hamster spleens as the tissue and rabbit serum in the liquid portion in place of hamster serum.

There are several biological strains of *L. tropica* They cannot be distinguished by culture or immunisation methods but only by their behaviour in sandflies *e g* the Palestinian strain of *L. tropica* multiplies readily in Phlebotomus papatasi but the Cretan strain is less infective for this Phlebotomus (ADLER, 1947).

Animal host

Apart from man, the dog and cat has been found naturally infected. There are many cases of cutaneous leishmaniasis in dogs in Baghdad

Aleppo, Teheran and Middle Asia (former Russian Turkestan and Bukhara). In the dog the lesion is usually localized on the ears, nose and paws, *i.e.* the non hairy parts. *L. tropica* in the dog must be distinguished from *L. infantum*. In dogs naturally or experimentally infected with leishmania infantum there are the following skin manifestations: seborrhea, depilation and sometimes ulceration. The whole skin of the body including the unbroken parts is uniformly involved and contains infected macrophages. This is fundamentally different from the purely localized lesions of *L. tropica*. Leishmania cutanea in the dog is a self limiting disease. The lesions appear about October and in most cases are spontaneously healed by July. ADLER and THEODOR (1930) inoculated a volunteer with cultures from the lesions of a dog naturally infected with cutaneous leishmania and produced



305. Gerbil

typical oriental sores. The lesion from this volunteer transmitted to other volunteers also produced typical oriental sore. Apart from the dog and cat, a circus bear was found naturally infected with *L. tropica*.

During the past 10 years Russian authors have described natural infection in the following rodents: Rhombomys opimus, the gerbils Meriones erythrourus, M. meridianus (in a small proportion) and sousliks spermo-philopsis leptodactylus. The Russian authors have proved conclusively that in the desert regions of Middle Asia these animals act as a natural reservoir from which sandflies are infected and transmit the disease to other animals and to man. Investigations in the hot deserts in Central Asia had revealed numerous sandflies in the burrows of gerbils and ground squirrels in the sand desert

the burrows of tortoises in the loess desert, and holes occupied by wolves, jackals and foxes in the stone desert. The high humidity and moderate temperatures afford shelter from the extremes of summer heat and winter cold.

Infectivity for animals

In the laboratory the most suitable animals for inoculation are mice and the Syrian hamster cricetus auretus. The most suitable method of infecting mice is to inoculate a culture in the proximal part of the tail. Local lesions are often produced in two weeks and frequently visceral infection also In the Syrian hamster a generalized visceral infection is produced. Here there is no ulceration of the skin. There are laboratory records of infections of the following animals dogs cats, monkeys, guineapigs, gerbils and rats (inoculated in the testicles)

Relation to other leishmaniasis

L. tropica can be distinguished by agglutination from *L. Donovani* *L. infantum* and *L. braziliensis* NOGUCHI (1926) found that serologically *L. tropica* can be distinguished from *L. Donovani* and *L. braziliensis*

Transmission

In culture *L. tropica* assumes a leptomonas form. The genus Leptomonas is widely distributed among insects including biting insects, *e g* fleas, sandflies and mosquitos, which itself indicates that there is an insect vector of *L. tropica*. During the last 40 years many insects have been suspected of being vectors, but the search for a vector must be limited by two considerations (1) The geographical distribution of the vector must be almost the same as that of the disease. (2) The insect vector must have a sterile alimentary canal because the cultural form of *L. tropica* does not survive in the presence of bacteria. It is now clearly established that the genus phlebotomus contains the vectors of *L. tropica* There are no foci of *L. tropica* in the absence of phlebotomi.

SINTON noted that in India the distribution of Phlebotomus sergenti corresponds to that of leishmania cutanea.

WENYON (1911) found in Aleppo sandflies naturally infected with leptomonad flagellates. In the light of what is now known it is obvious that he actually observed *L. tropica* in wild sandflies.

SERGENT *et al.* (1921) macerated ? sandflies caught in Biskra—an endemic centre of the disease. They examined the macerate and found no flagellates. Inoculation into a volunteer of the same material was followed by a lesion resembling leishmania cutis at the site of inoculation. ADLER (1925) found leptomonas in wild sandflies caught in Jericho—another endemic focus. ADLER and THEODOR obtained leptomonad flagellates by dissection of wild sandflies caught in Jericho.



306. Oriental sores.

They inoculated the flagellates into 3 volunteers. All 3 developed cutaneous leishmaniasis at the site of inoculation. Both wild and laboratory bred sandflies Phlebotomus papatasii were infected by feeding on experimental and natural lesions of cutaneous leishmaniasis.

Life history of L. tropica in Phlebotomus papatasii and in Phlebotomus sergenti

The Leishman Donovan bodies develop into flagellates in the stomach of the sandflies. They multiply and ascend the cardia (anterior portion of the midgut) towards the oesophageal valvae. The multipli-

cation may be so considerable that the anterior part of the midgut can be choked with flagellates. On the other hand flagellates are often absent from the hindgut even in the most intensive infection. The flagellates pass forward beyond the oesophageal valvae into the oesophagus pharynx and buccal cavity The two latter may be filled with flagellates In a small proportion of infected sandflies the flagellates extend as far down as the distal parts of the epipharynx. ADLER and BER (1941) produced 28 lesions of Leishmania cutanea in five volunteers by the bite of sandflies infected by feeding on a suspension of flagellates in defibrinated blood in 2.7 % saline They recorded



307 Typical oriental sore.

flagellates from the puncture wound caused by an infected sandfly Thus the transmission of *L. tropica* by sandflies has been established beyond doubt In the desert region of Middle Asia, according to Russian workers, Phlebotomus papatasii, Phlebotomus caucasicus and Phlebotomus sergenti breed in the burrows of wild rodents (gerbils and sousliks). The sandflies acquire the infection from these animals. It was here proved conclusively that naturally infected wild rodents serve as reservoir hosts of cutaneous leishmania. Sand flies breeding in the burrows of these rodents transmit the disease to man.



308 Oriental sore Vegetative or framboesiform type

Immunity

Natural immunity is rare. Occasionally attempts in the laboratory to infect a particular individual fail, but this transient immunity is not permanent. People living in endemic centres generally become infected only once in their lives and then are apparently immune.

The author has inoculated spontaneously cured cases with cultures of L. D. bodies. Strong local inflammation, often accompanied by rise of temperature, resulted. A leishmania sore developed in one case only. In this case there was an interval of more than 7 years between the two infections. It is popularly held that a person recovered from a sore in one endemic focus may receive a new infection in another endemic area.

There are several biological strains of *L. tropica* which can be distinguished by their infectivity for specific sandflies, but there is as yet no experimental evidence of cross-immunity. Russian authors working in Middle Asia recognize two aetiologically independent types of cutaneous leishmania, the "dry" urban form, and the "moist" rural form ("Pendeh"). They found no cross-immunity between the two types (KOJEVNIKOV, LATYSHEV and KRIUKOVA).

KOJEVNIKOV (1945) claims that inoculation of cultures of leishmania isolated from a source of one type protected against infection with homologous sores, but not against heterologous sores.



309 Oriental sores.

Mechanism of immunity

Nothing definite is known about the mechanism of the immunity whether it is cellular humoral or a combination of these two. The course of development of immunity has been investigated by many authors in connection with vaccination for experimental work or as a prophylactic measure It was found that as a rule, superinfection succeeded 3–4 months after the primary infection. Subsequently failures became increasingly frequent until after one year no re infection could be produced (BERBERIAN (1944), SENEKJI and BEATTIE (1941) SOKOLOVA (1941–1942)) Immunity develops slowly in man, sufficiently to control the natural infection after appearance of the sore, but not to prevent experimental superinfection with a large dose of L. D bodies

SYMPTOMATOLOGY

Incubation period

The incubation period can vary from one year to more. NAPIER recorded a case of 3 years' incubation. The average time of incubation in a natural infection is about 5 weeks.

During a vaccine campaign with more than 1000 inoculations with cultures with *L. tropica* the incubation period varied from a few days



310. Oriental sore, furunculoid type

to 18 months. The average period was 4–6 weeks (KATZENELLENBOGEN, 1944). SOKOLOVA in her large scale vaccination in Middle Asia (1522 vaccinations) recorded an incubation period of a fortnight to one year. SENEKJI and BEATTIE in their vaccinations with cultures found the incubation period 2–4 weeks in adults and about 2 months in children. The incubation period varies with the quantity of the inoculum, the depth of inoculation and individual susceptibility. It is even held that the incubation period may be absent clinically when large doses of flagellates are injected (DOSTROVSKY, 1946). Boils may

appear successively during a period of some weeks or even months. It is presumed that each boil represents a separate infection. As the incubation period may vary from several days to weeks or months new boils may appear during this period Hence different forms often corresponding to the duration of the boils are obtained.

Distribution of the boils

Oriental sore is common to all ages. It more often affects the uncovered parts of the body — the face, neck, limbs, but sores on the trunk, hairy scalp even the penis have been described.

Number of sores

Lesions are often single. In other cases as many as 300 and more have been counted upon the same patient. There are foci characterized by single or few boils, while in others multiple lesions are prevalent

Clinical descriptions

Definitions given by numerous authors for oriental sore hardly cover the description of the boils even in one region. The great variety of the clinical picture can only be compared with that produced by syphilis.

MARCHIONINI suggests an arbitrary division of the clinical forms into three stages The primary stage from the invasion of the parasite till the spontaneous healing of the boil, a period lasting a few months to a year The second period covering the cases where the parasites are spreading through blood (?) or lymphatic vessels. The third period includes all cases of the primary or secondary period who show no tendency to spontaneous healing These sores can last for years

RABELLO s division of the cutaneous leishmania includes (1) ulcerative boils (impetiginoid, ecthymatoid, true ulcers) (2) non ulcerative boils a) nodular-dermal b) vegetant (framboesoid or verrucose

Simple boils papules

The smallest leishmania boil is a bluish-red infiltration [illegible] to lentil size It is found only occasionally single or multiple [illegible] with other manifestations of leishmania. The papules [illegible]



311 Oriental sores.



312 Non-ulcerating leishmania-nodules.

months without scars and the bearer belongs later to those cases which are supposed to be immune to leishmania. The only common link between these insignificant papules and the extensive forms of cutaneous leishmania may be the presence of L. D. bodies in the smears

or in culture. The papules disappear spontaneously after a few months or grow to the size of a nut or olive They have the characteristic elevated margins of bluish-red colour The centre is either covered with glittering scales or it shows a tendency to ulceration. The granulations show but little tendency to heal and untreated last for about 6–12 months. The boils are either solitary or multiple. The blue red-blue colour of these solid indolent sores with glittering scales or



313. Cutaneous leishmaniasis furunculoid type.

an ulceration on the top are characteristic of cutaneous leishmaniasis. The majority of these cases are morphologically easy to recognize.

The nodular sores

The nodules of cutaneous leishmania are larger deeper and more infiltrated than the papules. They may last for many months and grow larger without any tendency to ulceration. This form is often regarded as atypical whereas the ulcerating variant is considered to be the typical form. LAVERAN (1917) described—under the heading

formes anormales"—these non ulcerating sores which terminate in resolution with or without retarded ulceration. THOMPSON and



314 Dry type: non-ulcerative papules.

BALFOUR (1910) have described cases of non-ulcerating oriental sores from Khartoum which they named "leishman nodules" KIRK (1942) also recognizes the two forms. CARTER (India), MANSON (Baghdad)



315 Oriental sore, moist type: superficial ulceration resembling tertiary syphilis.

and BERGAMESCO (Italy) report similar non-ulcerating forms. The writer has often seen this form in Palestine. It should not be confused

with a nodular condition called dermal leishmanoid which will be dealt with later.

L. D bodies are usually abundant in this form of cutaneous leishmania and the bacteriological diagnosis presents no difficulties.

Extensive sores

More diagnostic difficulties arise when the sores spread, cover areas of several inches across and assume various morphological forms.



316 Oriental sores place of predilection.

The dry white scales covering the boils may become moist, thick and brown. The ulcers extend by erosion. The sores may assume the character of a tubero-serpiginous granulation and resemble a late syphilis lupus vulgaris or even blastomycosis. If the spreading is not ulcerative but rather infiltrative the adherent crusts remain dry and the appearance of the sores is that of a lupus pernio or lupus erythematosus. Clinically the bluish-reddish colour is often helpful in the diagnosis of these cases. These forms are not rare in certain foci

while they never appear in others. The search for L. D. bodies is often difficult in these cases. Diagnosis can be confirmed by cultures or intradermal reaction, which is usually positive.

Results of histological examinations are not conclusive.



317. Oriental sore of the lip.

Leishmania recidivans

Of special clinical interest is a form of cutaneous leishmaniasis recently named relapsing leishmaniasis. The clinical and histological resemblance of this form to lupus vulgaris is striking. The difficulty of finding L. D. bodies in the smears and the histological structure led numerous authors to regard this form of cutaneous leishmania as lupus vulgaris in the site of healed oriental sore (GOUGEROT, SINDERSON, BLIGET, NOGUER MORÉ). The lesions either persist as sequelae of ordinary leishmaniasis or develop as new lesions on the site of the old scars. They vary in size from that of a pinhead to that of a lentil. Their surface is either smooth or covered with tiny adherent whitish scales. The lesions are firm but flat. Their colour varies from yellowish-brown to reddish bluish-violet. The papules are discrete or coalesce into small plaques or rings. They involve the borders of the scars but do not spare the centre. The papules may form a ring or have a semi



318–319 Oriental sore erythematosus-form.



320 Leishmaniasis recidivans.

circular or serpiginous distribution around the previous scars. The condition remains unchanged for years or progresses very slowly The diascopic examination often reveals applejelly-coloured dots.

I have seen a case of 16 years duration. Gitelzon reported a case of 31 years duration

This form is not identical with the lupoid form of cutaneous leishmaniasis. Leishmania recidivans develops only after healing or apparent healing of the primary leishmania sore and is not necessarily limited to its scars (DOSTROVSKY SAGHER KATZENELLENBOGEN).

The patients are usually young persons. SINDERSON stresses that this condition is fairly common among young children in Baghdad and mention is made of one family in which four out of five children suffered from oriental sore complicated by lupus vulgaris. SINDERSON has not seen this condition in adults nor in European children. The author has seen European children from Baghdad and Teheran with





3 1 3— Leishmani recidi an

this form of leishmaniasis. The face is more often involved but there are cases affecting the limbs. DOSTROVSKY SAGHER described a case of generalized recurrence in leishmaniasis. The patient—a 10 year old girl—from Aleppo suffered from multiple skin lesions due to leishmania infection. These lesions healed but 4 months later fresh lesions began to develop at the original foci and continued to do so till complete relapse of the original condition had occurred.

The histological examination of this form shows tubercles composed of epithelioid cells and giant cells. Between the tubercles there is often a round cell infiltration.

Examination with GIEMSA or LEISHMAN stain fails to show the parasites.

Culture methods are often necessary for diagnosis. As a rule this culture takes 3–4 weeks in comparison with one or two weeks in the case of the ordinary boil.

A second important diagnostic aid is the Leishmania vaccine-test. The intradermal injection of 0.1 ml of a culture containing a suspension of 100 000 flagellates elicits 2 days later a very strong positive reaction at the site of the injection. DOSTROVSKY believes that this form is a result of disturbance of immunity, improper treatment or lack of resistance in asthenic individuals.

Inoculation with a culture obtained from a leishmania recidivans



323. Verrucose form of cutaneous leishmaniasis



324. Rhinophymatous or verrucose cutaneous leishmaniasis

case produced an ordinary leishmania boil without any tendency to the relapsing form (KATZENELLENBOGEN 1944).

This relapsing form with practically no parasites in the smear ("Leishmaniasis sine Leishmania" VILANOVA) with a few lymphocytes, no plasma cells and numerous reticulum or giant cells is therapeutically the most obstinate form of oriental sore. It is usually seen in old endemic centres (Baghdad, Teheran, Istanbul, Turkmenistan etc.).

The vegetant sore (framboesoid or verrucose)

Individual immunological reaction of the skin to the leishmania infection combined with secondary infection may lead to peculiar verrucose forms of the sores. On the nose it may resemble rhinophyma, on the limbs vegetant cancer. The inflammatory background is concealed by hypertrophic crusts. The elementary nodular or ulcerative lesions are not visible. Only the bluish red colour of the margins may be helpful in the clinical diagnosis.

Leishmania of the lips and eyelids

Only exceptionally are lips and eyelids affected. The lip may show an elephantiastic hypertrophy. Only the borders show the charac-



325. Leishmaniasis of the lip and the lower arm

teristic bluish red colour. The vermilion usually remains free. Satellite adenopathy is of no significance. The sore on the lip may resemble a primary sore, while in aged patients leishmania ulcers of the lip or eyelids particularly when the borders are infiltrated are difficult to distinguish from cancer of the skin.

Cutaneous leishmaniasis *on the eyelids* shows different forms: the

red-bluish-red nodule with a scaly top or the ulcerated sore leading to swelling of the eye. Secondary infection with staphylococci and streptococci may lead to scars and ectropium of the lids. NAPIER and others (1942) described a case of involvement of the cornea in dermal leishmaniasis.

A *verrucous form* was first described by FERGUSON and RICHARD in Egypt. The size of the plaque varies greatly. Its outlines are well defined and it is situated on healthy or slightly erythematous skin.



326. Cutaneous leishmaniasis resembling eczema.

The lesion is raised and whitish grey. It presents a uniform surface; it begins and ends on healthy skin. Its site of election is the lower limbs. It usually occurs in neglected cases.

Squamous eczema of the back of the hand is sometimes imitated by leishmania. The lack of any pain or itching, the bluish-red colour of the involved skin, and the presence of organisms in the smears will decide the issue.

Leishmania ulcer on the ankle with elevated edges and crateriform appearance may resemble a tropical ulcer. The smears, however do

not contain spirochetes and bacillus fusiformis. L. D. bodies can be found in the bluish edges of the ulcer.

Dermal leishmanoid or post-kala-azar leishmaniasis

The term "dermal leishmanoid" was introduced by BRAHMACHARI (1922) to indicate certain skin lesions due to infection of the skin by *L. donovani*. This skin eruption is a sequela to generalized infection with *L. donovani*. The characteristic lesions appear in individuals apparently cured of kala-azar. In India the skin lesions appear after a latent period of 1-2 years (NAPIER and others), in the Sudan immediately after the completion of treatment (KIRK).

The eruption is always prominent on the face, where it appears first, usually on the forehead or malar region. The distribution may be limited to these regions or the whole face and neck may become involved. Less commonly the eruption appears on the limbs and trunk.

Clinical features

The following clinical types have been described:

1) Macular rash
2) Papular eruption
3) Nodular eruption
4) Verrucous or papillomatous eruption.

In the Sudan KIRK described a minutely punctate rash. In a number of cases the cutaneous manifestations may pass through a stage of depigmentation before finally disappearing.

The lesions on the face, but rarely on the body, may change from the papular to the nodular form.

The nodules are soft, granulomatous growths about the size of a split pea. They may join and form plaques. Again the nodules may change and appear as verrucous or papillomatous growths. There are no subjective symptoms such as itching or burning.

Dermal leishmanoid usually occurs in treated cases. Only exceptionally does the condition appear in cases with spontaneous recovery from visceral leishmaniasis. The lesions may be inconspicuous yet persist for a very long time. General health is unaffected and there is little tendency to visceral relapse. Leishmania parasites are usually

abundant in the papules and nodules They are rarely found in the erythematous and depigmented areas. At this time parasites are not found in the visceral organs or in the blood. NAPIER and DAS GUPTA believe that patients with dermal leishmanoid may constitute a low grade source of infection with kala-azar Sandflies have been infected by feeding on dermal lesions, not only on nodules but also on depigmented areas A patient with dermal leishmanoid may be regarded therefore practically as a carrier

Association of kala-azar with oriental sore

KIRK in the Sudan described cases where visceral, cutaneous and mucosal lesions were present in the same individual. KIRK suggested that different strains of leishmania exist, varying in virulence with different degrees of dermatropic or viscerotropic tendency The biology of leishmania infections provides some basis for the assumption that strains in different regions will tend to vary more or less from each other

PATHOLOGY

The histological picture differs according to the stage of the infection and the clinical type. We must not expect a uniform histological picture. There are fundamentally two components in the cellular reaction caused by *L. tropica* primarily a local proliferation of reticulo-endothelial cells, forming a syncytium, and secondarily a round cell and plasma cell infiltration. The simple cellular reaction is gradually replaced by granulation tissue having a tuberculoid structure These components occur in different proportion in the various stages of the same infection. Local proliferation of reticulo-endothelial cells may be the only cellular change found in the earlier stages of an experimental infection. The L D bodies multiply extensively in these cells Later there is in addition a round cell and plasma cell infiltration after which the number of parasites in the reticulo-endothelial cells diminishes till finally they are too few to be detected in smears. Parasites gradually disappear and the lesion resolves. Immediately above the area of intensive reticulo-endothelial infiltration the epidermis may be ulcerated

The lesions may then be subjected to secondary infection and the

typical histological picture of leishmania is then complicated by secondary infiltration with polymorphs. The papillae above the area of intensive infiltration are atrophied but on the margins of the infection they usually hypertrophy and cell pearls may be found here. In a few cases the round and plasma cell infiltration may dominate the picture from the very beginning of infection. The presence of giant cells makes the lesions resemble lupus vulgaris and in these cases parasites are few or none. Diagnosis can only be established by culture.

In Leishmania recidivans it is the round cell infiltration, histiocytes and giant cells which dominate the histological picture. The number of parasites in these cases is usually too low to be detected by smears.



327 Oriental sores with elevated indurated borders.

They can be diagnosed only by culture and by skin test. Histologically these lesions are often indistinguishable from lupus vulgaris and have often been diagnosed by experienced pathologists as such.

Pathology of dermal leishmanoid

In a section of the nodules NAPIER found oedema of the subpapillary layer and dilatation of the vessels. The fibrous and elastic tissue were atrophied. Below the oedematous area was a granulomatous mass with proliferating macrophages and fibroblasts. In the centre of this mass were multinuclear cells packed with L. D. bodies.

DIAGNOSIS

In view of the large variety of clinical forms a correct diagnosis can only be established by demonstrating parasites in stained scrapings of the lesions by cultures, or by biological reaction (skin test). Smears are best obtained by pipette aspiration at the periphery of the lesion. A negative finding in stained smears should not exclude a diagnosis because in some lesions parasites are too few to be found by direct microscopical examination. In case of a negative smear cultures should be made and kept for at least 3 weeks before they can be considered negative. In endemic centres cases resembling lupus vulgaris should always be examined by culture methods for *L. tropica*. Because of their clinical appearance a number of cases have been regarded as lupus.



328 Oriental sores. Vegetative form.



329 Verrucous form of cutaneous leishmaniasis.

Skin tests

MONTENEGRO (1926) first recommended an intradermal test which can be employed as an auxiliary diagnostic method for cutaneous leishmaniasis. It consists in the allergic response of the skin to intracutaneous inoculation of an antigen. The vaccine is usually a phenolized

saline suspension of a flagellate culture 0.1 ml containing 100 000 parasites being injected In a positive reaction there appears after 24 hours a reddish papule which gradually increases in size The reaction reaches its full development after 2 3 days It is particularly strong in cases resembling lupus vulgaris *i.e.* cases of recurrent and tuberculoid leishmaniasis when 98 per cent positives were obtained (DOSTROVSKY -SAGHER). A positive leishmania test can be obtained within a few days of the development of the sore The sensitivity to the leishmania test appears to remain for many years afterwards. ADLER observed this reaction 22 years after spontaneous cure. SAGHER has used graded intracutaneous doses of leishmania vaccine The same dose that in one person provokes a necrotic reaction may in another elicit only a very weak response While in case of *leishmania tropica* the reaction was positive to a dilution 1 10 of the original vaccine it was in cases of *leishmania recidivans* still positive in dilution 1 10 000 of the original vaccine

In endemic areas certain persons may show a positive reaction to an intradermal leishmania test without exhibiting sores or scars of leishmania. It is presumed that they have had an inapparent infection with leishmania in the past

Leishmania and syphilis

Leishmania cutanea of long duration can easily mimic the basic characteristics of late syphilis. "It is impossible in studying the various cutaneous granulomata to escape the belief that there are certain fundamentals of bodily reaction to all the granuloma producing agents which are present alike in syphilis lepra tuberculosis, sporotrichosis and blastomycosis infections. Diagnosis must be made by preponderance of evidence" (Modern clinical syphilology 1944)

T this list leishmania should be added and in warm countries should be the first to be considered

Grouping of leishmania lesions, annular or circinate configurations, bring syphilis into the differential diagnosis As in syphilis the healing is central. Unlike syphilis metastatic nodule formation can appear in cutaneous leishmaniasis beyond the periphery The resemblance to syphilis is also present in ulcers with a punched out appearance These forms may lead to deep tissue destruction. These lesions are

more common on the legs They grow slowly they last longer than the usual type, and they heal more slowly even under X ray treatment. Secondary infection may with time cause evil smelling pus under the crusts

A third syphilis-like form of cutaneous leishmania has the appear ance of a rupia. The indolent ulcer is covered with crusts through



330 Leishmaniasis recidivans resembling tertiary syphilis.

successive accretions from below As the lesion enlarges a lamellated pyramidal hardened mass gives the boil an oyster shell-like configur ation.

Leishmania and tuberculosis of the skin

The hypertrophic type of lupus vulgaris, lupus tumidus and vege tative tuberculoma may be closely imitated by leishmania. The ver rucous adherent scaling may recall tuberculosis verrucosa cutis.

Leishmania may further imitate *tuberculosis colliquativa cutis* The bluish red soggy inflammatory skin with a tendency to ulcerate appears on the neck or near the ear with involvement of the local glands Few authors have succeeded in tracing *L. tropica* in the glands. The spread of leishmania from the primary boil through the lymphatic vessels and the formation of new boils in the vicinity has been des-

cribed by several authors (LAVERAN, COTTINI, VIONT, POGGIOLI). The usual type of this form is lymphangitis. It may resemble a string of pearls with nodes of different size. MASSON BAHR described enlargement of the lymph-nodes situated in the drainage area of the sore. Secondary lesions may appear along the course of lymphatic channels (DOSTROVSKY, MARCHIONINI). When the primary sore steadily grows through infiltration a lupus tumidus like picture may result. When the ridge of the nose and infraorbital region are involved,



331. Experimental or vaccination leishmania sore

the bluish-red colour, the adhering scales and the butterfly distribution may recall lupus erythematosus.

Parasites are more regularly found in these cases, even if they have lasted several years and shown no tendency to heal. The long duration may, however, lead to secondary infection. The sore is covered with crusts and the chances of finding leishmania parasites are decreased.

Leishmaniasis and leprosy

MUIR has called attention to the possibility of mistaking dermal leishmanoid for leprosy. Cases with depigmented skin areas and nodular or xanthoma-like lesions have been treated for leprosy.

THERAPY

1 *Cutaneous leishmania*

No single line of treatment can be expected in a skin condition with such a variety of clinical forms as cutaneous leishmania. Each case must be treated individually according to its merits. Experience shows that best results are obtained in those cases where parasites are abundant in the smear and plasma cells in the histological section. Cases with a few parasites in the smear and increasing number of epithelioid cells in the histological tissue are more resistant to treatment The greatest difficulty is experienced in the treatment of the relapsing form with practically no parasites in the smear On account of the benign nature of the sores it is doubtful whether antimony compounds, which are highly recommended by many clinicians, should still keep their favourite place in the treatment of cutaneous leishmania. Where possible particularly in single boils of nodular papular furuncle like appearance, local treatment should be preferred.

Local treatment

1) *Paints* a. Small lesions can be treated by painting with brilliant green (tetraethyldiaminotriphenylmethane silver, or CASTELLANI paint.
b. MANSON BAHR s cignoline paint.

Rp	cignoline	0.25 g
	ichthyol	0.50 g
	ol. cadini	2.50 g
	benzol rect.	28 50 g

The paint is applied daily to the whole area of the sore but not to the surrounding skin, by means of a camel s hair brush after through cleansing of the sore

For more chronic types MANSON suggests cignoline ointment.

Rp	cignoline	0.25 g
	zinc. oxide	14 g
	ol. olivae	14 g

c. "Cretan" paint powdered vegetable charcoal in concentrated sulphuric acid 1 10 The wet powder is applied to the sore with a glass stick. This method has been useful scars and keloids may result if the lotion is applied too freely

2) *Scraping.* A method advised by Indian authors is that of scraping the sores followed by application of pure carbolic acid. The sore is then covered directly with elastoplast or ordinary adhesive plaster. The plaster is left in situ for 14 days. SHAH (1942) advised scraping followed by dressing with tannic acid powder or magnesium sulphate paste.

3) *Injection into the boil.* Different medicaments have been recommended for injection into the circumference of the sore.

a. 1–2 per cent. solution of *berberine acid* sulphate. 1 ml is injected into a single sore from several points. The process is repeated every other day (CHATTERJEE, 1934) or at weekly intervals (KARAMCHANDANI, 1930). The total number of injections does not exceed 12. No more than two sores are treated at one sitting. This treatment is rather painful.

b. PHOTINOS (1918) introduced emetine for injection into the boil. A one per cent. solution is used. The quantity injected varies from 0.01 to 0.12 cc. The total dose should not exceed 1 gram. The needle of the syringe is inserted into the circumference of the boil and if the injection is succesful the skin round the sore becomes red.

c. Quinacrine (Atebrine) (FLARER, 1938) is the most popular injection into leishmania boils. The usual dose is 0.05 to 0.1 g. dissolved in 1–2 ml. of distilled water. This may be increased at subsequent sittings to 0.3 g. The treatment has to be repeated once or twice at intervals of 9–10 days. Strong pressure or too large a quantity of injected liquid should be avoided, as it may lead to local necrosis of the skin. This applies particularly to boils on the nose and ear.

This treatment is particularly suitable for lesions on the face (MARCHIONINI, FLARER).

d. Solustibosan has been used for injections into the base of the sores by VILANOVA (1943). The dose employed is 0.4 ml per 10 kg. of bodyweight. A total dose of 2 ml must not be exceeded.

4) *Sulphonamides.* Ulcerated oriental sores have been treated by local application of sulphonamide derivatives. The powdered drug is applied directly to the sore after cleansing with saline solution (MILIAN, AKRAWI) (Beware of sensitization!).

5) *Carbon dioxide.* Carbon dioxide was first introduced by BROOKE

(1911) for single sores. The application gives good results with small sores or nodules.

6) *Electrocoagulation.* BEHCET, HIGOUMENAKIS and others favour electrocoagulation. The method yield good results with small nodules or papules. It is useful in cases of relapsing leishmaniasis. The writer prefers unipolar application to avoid keloids. This method should be avoided where there is extensive ulceration; the tendency of dark coloured patients to keloids should also be kept in mind.

7) *X Ray treatment.* The best treatment for extensive sores and those of long duration is the application of X rays or Grenz-rays.





332, 333. Vegetative form of cutaneous leishmaniasis resembling cancer, before and after X-ray therapy

This treatment represents a distinct advance. It is absolutely painless unlike most of the previous methods. It can be applied in all stages. It gives good results in 90 per cent. of cases. The older the case the more marked is its susceptibility to X rays. Leishmania recidivans is the only exception. For advanced cases 250 to 300 r, have been used, while for early ones 400–600 r (DOSTROVSKY-DREYFUSS 1936).

Technique of radiation: 3 Al. filter, 150 kV, 6 mA and 30 cm. focal distance from the skin. If definite regression is noted treatment is given only once. Otherwise the same dose is repeated. Only exceptionally is a third irradiation necessary. Healing takes 4–15 weeks. Each lesion has to be radiated separately as the effect of the X rays is only local.

MARCHIONINI (1943) used only 50 r. with 0.5 mm. Cu filter 160 KV. repeating this radiation every 10 days.

Grenz-rays. Two exposures of 800 r. with half value layer of 0.027 mm of Al. are given in the usual type of oriental sore (DOSTROVSKY and SAGHER 1942). The authors claim good results in the chronic relapsing form (3 000 to 11 000 r. with half value layer of 0.02 mm of Al.)

General treatment

Organic antimonials are still favoured in cases where there are numerous sores. VIANNA (1913) first introduced tartar emetic (sodium antimony tartrate) intravenous injections in the treatment of South American muco-cutaneous leishmaniasis. It has since been used in the treatment of oriental sore. The solution of antimony should be made up freshly. 1–2 per cent. solution is used. Injections are given every third day. Ten injections are the usual course. Of the pentavalent compounds neostibosan (neostam) is given intravenously. Doses commencing with 0.05 g. are increased on alternate days to 0.2 g. In cases with a toxic reaction the dose should not exceed 0.15 g. Quantity given to each patient averages 1.2 g. Toxic reaction appearing after intravenous antimonial injections consists in mild nausea, vomiting and collapse. Morphine hypodermically gives relief.

Of the trivalent antimony derivatives for intramuscular treatment anthiomaline, fouadin and tantorin have been used by various clinicians. PIZILLO has described three cases of cutaneous leishmaniasis which were only cured after a co-existing malaria was also treated. He termed this type "*palu-leishmaniasis*".

Gold injections

Gold preparations have been used chiefly by Russian authors. (GHELIZON, SOBINSON (1932), KRASSNJANSKIJ and LAWROW (1936). They have reported good results by intravenous injection of Krysolgan, Solganol, Sanocrysin and other gold preparations. KRASSNJANSKIJ and LAWROW observed as a rule an acute reaction around the sore after 2–5 injections. Complete healing has taken place after 10–15 injections.

Penicillin has no effect on cutaneous leishmaniasis (SNOW, HALAWANI

JALLIL) but may help to clear the secondary infection of the boil (ELEKTON).

Vaccine-therapy of cutaneous leishmaniasis was first tried by Row (1912) The vaccine is a saline suspension of washed flagellates killed by heat. It contains 1.5 million flagellates per 1 ml 0 1 ml is injected intradermally The course consists of up to 20 intradermal injections. DOSTROVSKY observed painful sterile abscesses develop at the site of the injections. DUBOVSKY reported local reactions, lasting 3–5 days manifested by redness, swelling, pain and increased discharge from the ulcers. DUBOVSKY achieved complete cure in 57 9 per cent. of cases treated.

2. *Dermal leishmanoid*

Certain cases of post—kala-azar dermal leismaniasis respond to antimonial treatment as readily as do ordinary cases of kala-azar while others are absolutely resistant. The pentavalent Neostibosan has proved to be more effective than sodium antimony tartrate MUIR advocates "as the only satisfactory method" intravenous injections of a pentavalent antimony compound

Prophylactic vaccination

Vaccination against cutaneous leishmaniasis with living cultures or directly from human lesions gives protection against numerous and disfiguring sores. Vaccination is now a recognized prophylactic procedure It has considerably reduced the incidence in certain hyper endemic regions (LAWROW and DUBROVSKY SOKOLOVA KOJEVNIKOV KATZENELLENBOGEN).

The writer has used suspensions of cultures on Locke Serum Agar of *L. tropica* isolated from local patients. Inoculations were made on the anterior surface of the thigh about 10 cm above the knee. One tenth cubic cm (containing approximately 1,500 000 active flagellates) of a culture suspension is injected intradermally Vaccination should be timed to bring about the final phase of the disease before the advent of the epidemic season. Russian authors consider that the amount of immunity acquired before the termination of the process is sufficient to reduce considerably the severity and duration of superimposed infection. The author had the same experience

Control

Protection from sandflies while living in an endemic centre is the most effective measure. This can be achieved by the use of sandfly nets but still better by spraying D.D.T. in living quarters, in using





334. Diffuse lupoid leishmaniasis before and after cure
(Drs. Pani)

insect repellents when protection for a number of hours is required. In Middle Asia where desert sandflies breed in the burrows of wild rodents, poisoning of the rodents is the most promising method of combatting the moist cutaneous leishmaniasis (LATYSHEV and KRIUKOVA).

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CHAPTER 12

AMERICAN LEISHMANIASIS OR LEISHMANIASIS MUCO CUTANEA

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DEFINITION

American leishmaniasis or leishmaniasis muco-cutanea is a specific granuloma affecting the skin and mucous membranes and caused by *Leishmania braziliensis*. A large number of synonyms coupled with a variety of clinical pictures tends to add confusion to this already complicated disease.

The names most frequently used are *Bahia ulcer* or *Bauru* in Brazil, *forest yaws* in British Guiana, *bosch yaws* in Dutch Guiana, *pian bois* in French Guiana, *Chiclero ulcer* in Mexico and *uta* and *espundia* in Peru. The last two names are not just synonyms, but are used, in certain areas to indicate different forms of the disease, as will be discussed later.

HISTORY

Figures on earth jars of the Incas show destruction of the nose suggesting that muco-cutaneous leishmaniasis may have existed already in those days. In 1826 TELLO mentioned boils caused by mosquitoes, leading to destruction of the face. FRAY HIPOLITO was the first to report a case in Brazil in 1827. As early as 1852, BRAVO noted the similarity between the uta form in Peru and oriental sore, an observation which was again made by VILLAR in 1859. ALEXANDRE CERQUEIRA identified the disease in 1885 in the vicinity of Bahia and suspected phlebotomus as a vector. The most important finding was

made in 1909 when LINDENBERG and shortly afterwards CARINI and PARANHOS were able to find a parasite in a case of Bauru ulcer in Brazil which they considered L. tropica. In 1911 VIANNA called this organism L. braziliensis and postulated its specificity in causing American leishmaniasis.

AETIOLOGY

American leishmaniasis is caused by *L. braziliensis* which is morphologically and in its cultural behaviour indistinguishable from L. tropica, the causative agent of cutaneous leishmaniasis or oriental sore and from L. donovani causing visceral leishmaniasis or Kala Azar. Clinically there are several marked differences between oriental sore and American leishmaniasis: the latter shows frequent mucosal involvement with subsequent severe destruction, long duration of all lesions (cutaneous and mucosal), a greater resistance to therapy, a longer and varied course and failure to produce immunity. LAVERAN considered L. braziliensis a variety of L. tropica and suggested, therefore, the name *L. tropica var. americana*. VIANNA regarded American leishmaniasis as a distinct disease entity; support to this theory was added by NOGUCHI who was able to show in agglutination experiments in sensitized rabbits that L. braziliensis and L. tropica showed serological differences. However, recent serological studies point to the presence of common and specific antigens in all the strains of leishmaniae. Antiserum against any one organism agglutinates the homologous organisms to a high titer while the heterologous organisms are agglutinated to a much lower titer. The intradermal test for leishmaniasis shows definite cross reaction, injections of antigen obtained from L. tropica giving positive results in American leishmaniasis and those obtained from L. braziliensis in oriental sore. All this speaks for a very close relationship of the two clinical groups, which might possibly be explained by different strains of the same parasite. KIRK stressed the many factors common to visceral leishmaniasis, Old World cutaneous leishmaniasis and American mucocutaneous leishmaniasis.

For practical purposes, however, it seems advisable to discuss American leishmaniasis separately from oriental sore because of the above-mentioned clinical differences. As regards the morphology of

the parasites and their behaviour in culture the reader is referred to the respective chapters in KATZENELLENBOGEN's *Cutaneous Leishmaniasis*"



335. American leishmaniasis (bush yaws) in a Surinam Negro (South America). (*Lars-Carneiro*)

IMMUNITY

American leishmaniasis does not confer permanent immunity in contrast to oriental sore This is one of the important points of difference between the two

forms of leishmaniasis, although it should be remembered that re-inoculation is possible also in oriental sore if different strains are used.

EPIDEMIOLOGY

American leishmaniasis is observed mainly in South America and, to a lesser extent, in Central America. Brazil and Peru are the countries with the highest incidence, but it is also endemic in Argentina,



335a The framboesiform appearance of bush yaws.
(Simons, Amsterdam)

Bolivia, Colombia, Costa Rica, Guiana, Guatemala, Martinique, Mexico, Panama, Paraguay, Uruguay and Venezuela.

American leishmaniasis is distributed unevenly, certain regions in one country being heavily infested while others are completely free. Sporadic cases have been observed in other countries, for instance in the United States, but most if not all of these were imported from an endemic area.

The unevenness in distribution is very similar to that found in oriental sore. American leishmaniasis is a disease of hot climates

and is most frequently found in densely overgrown areas, especially in virgin jungle and at a low altitude however it is encountered also at altitudes of 1 000 to 3 000 meters on both slopes of the Andes

American leishmaniasis is most likely transmitted by flies of the genus *Phlebotomus* In 1922 ARAGAO fed phlebotomus intermedius on ulcers of American leishmaniasis, found flagellates in the flies and inoculated their intestinal contents into the nose of a dog Three months later ulcerations formed at the site of the inoculation and leishmaniae could be demonstrated in them. Other insects besides phlebotomus have been incriminated, for instance the mite *Trombicula flui* and certain ticks and simulium, but as yet there is not enough evidence to prove that they serve as vectors. Direct contact from man to man seems to account for some infections. Natural infection in animals is rare. It has been observed occasionally in dogs in Argentina, but much less frequently than in regions where oriental sore is endemic. Experimentally dogs cats monkeys and guinea pigs were successfully inoculated with L. braziliensis. It seems that small animals are less susceptible to L. braziliensis than to L. tropica.

INCUBATION

The incubation period in natural infection of American leishmaniasis varies greatly averaging from 2—3 months. However it should be stressed here that the time interval between the appearance of the cutaneous lesions and that of the so-called metastatic mucosal involvement can be as long as 15 years

SYMPTOMATOLOGY

The great variety of clinical manifestations encountered in American leishmaniasis is well demonstrated in the classic classification by RABELLO

I *Cutaneous*
- A. ulcerative
  - a. impetiginoid
  - b ecthymatoid
  - c. true ulcerative
- B non-ulcerative
  - a. nodular dermal
  - b vegetating frambesiform or verrucous

II *Subcutaneous*
  A non ulcerative: nodular hypodermic
  B ulcerative (secondary): nodular ulcerative
III *Mucosal*
  A non ulcerative: vegetating
  B ulcerative: ulcero-vegetating
IV *Mixed*
  Combination of the above-mentioned forms



336 American leishmaniasis. Ulcerative type with small vegetations in the base. *(Simons—Amsterdam)*

A simpler classification differentiates between a cutaneous, mucosal and mixed form and subdivides the mucosal form into a primary and a metastatic form. GOLDMAN gives the following basic formula for the development of the lesions:

Inoculation → papule ⇄ ulcer → scar

The earliest lesion of the cutaneous form is often a papule which develops at the site of an insect bite and is usually located on an exposed surface like the face neck, ears, arms, or legs. Scalp, palms and soles are rarely affected, but the external genitalia, especially penis, scrotum, and labia can be the site of lesions The primary papule slowly increases in size and becomes crusted. From then on the development may be in two fundamentally different ways. Either the papule enlarges and eventually becomes the nodular form, or it starts



337 American leishmaniasis at the inner aspect of the thigh.
(Rev and Hambe-San F series)

to ulcerate at an early stage. If the lesion ulcerates, its floor becomes covered with a dirty yellowish membrane under which there is easily bleeding granulation tissue. Smaller lesions may show firmly adherent crusts. Sometimes there is no actual ulceration in the beginning, but one sees a moist area covered with a membrane. The ulcers may have a punched out appearance.

The non-ulcerative lesions have elevated borders and a crateriform centre. Later they may develop into papillomatous or verrucous

formations. Cauliflower-like lesions are occasionally seen and may remain for years. These lesions are sharply demarcated and have an irregular, fissured surface.

The number of cutaneous lesions varies greatly. They can be single but are often multiple. In rare cases, several hundreds have been observed in a single individual. In most cases, the generalization is caused by auto-inoculation (no immunity), but occasionally it can be due to multiple infection or lymph spread.

The cutaneous lesions have a tendency to heal spontaneously



338. American leishmaniasis. Verrucous type, resembling a "mossy foot." (Orig. G. Castro-Belo Horizonte)

although they persist for years. When healing, the elevated borders of the nodules flatten first and the floor of the ulcers becomes clean.

The ulceration in the ulcerative form is not due to secondary infection, although secondary invaders are practically always found in the ulcers. The reason why certain individuals develop either the nodular or the ulcerative form may be one or a combination of the following: constitutional set-up, state of resistance, defense mechanism of the body, or an inherent difference in the organism.

In the so-called *lymphangitic type* nodules which eventually ulcerate appear along the lymphatics of an extremity resembling the clinical picture of sporotrichosis.

Osteitis has been observed in bones underlying cutaneous lesions, but seems to be rare. The *lymph nodes* are often enlarged, even if there is no noticeable involvement of the lymphatics. General symptoms are rare. Occasionally there is fever, headache, or joint pain.

The *mucosal lesions* may either originate from skin lesions around the mouth or nose which grow without break in continuity into the mucous membrane, or they can appear months or even years after the skin lesions started and be in an entirely different region.

ESCOMEL called the first form *uta*. It often starts on the skin of the face, very much like oriental sore. However its growth does not stop when the mucous membranes are reached, but continues into them. Its course is relatively mild and it is less destructive than the second form.

Espundia is the name used by ESCOMEL for the second form of mucosal involvement, which begins 8 months to 15 years or more after the appearance of the original skin lesions. The latter may have healed in the meantime. The mucosal lesions usually develop far away from the original skin lesions. This fact and the long time interval makes many observers think that they are of metastatic origin. Therefore this form is often referred to as the metastatic form. The metastatic nature of these lesions has not been proved. The idea that visceral involvement does not occur—which was one argument against this theory together with the absence of parasites in the blood stream—may be disproved by further investigations. Leishmaniae have been demonstrated in lymph nodes and BORZONE found them in material obtained from the spleen. Espundia corresponds roughly to the ulcero-vegetative form of RABELLO. It affects the nose, nasopharynx, lips, palate, tonsils, larynx, trachea, bronchi and oesophagus, but rarely the tongue. It often begins with an oedematous swelling; later soft granulation tissue forms. The infiltration increases gradually. There is no tendency to early ulceration. The nasal septum is soon destroyed, both membraneous part and cartilage; however the bone usually remains unaffected. Occasionally two deep furrows are seen on the palate, forming a cross; this is called crux palatina or palatal cross of espundia.

Espundia is characterized by a slow progressive course which usually leads to severe mutilation and may end in cachexia and death. There is little tendency to spontaneous cure Interestingly these so-called metastatic mucosal lesions which are thought to originate from the skin, may again spread into the skin from the mucous membranes by continuity

The percentage of mucosal involvement varies considerably in different regions the highest figure reported being 80 % the average figure seems to be 20 % In Brazil and Paraguay it is seen mainly in men working in forests and jungle at an altitude of 400 to 600 meters



339 Chiclero ulcer in a chicle collector
(Fasal & Graber San Francisco)

and starts usually during the rainy season while in Peru it occurs also at high altitudes

The names *uta* and *espundia* for the above-described types of mucosal involvement originated in Peru and are understood and used in the same sense there and in several other South American countries, but by no means in all In Brazil, for instance which has the highest incidence of American leishmaniasis, these names are not used. On the other hand the name espundia is being applied to American leishmaniasis in general A more unified terminology is advisable

In Mexico and Guatemala American leishmaniasis occurs in the form of the so-called chiclero ulcers In 85 % of the cases these are located on the ear lobes and begin as a dark red papule, which is often oedematous. A scab forms and a shallow ulcer develops. There can be considerable sloughing of the ear. *Chiclero ulcer* is found mainly among the workers collecting chicle from rubber trees in the Yucatan peninsula. The ears are especially exposed to insect bites No mucosal involvement is seen in these cases.

Among the rarer pathological conditions caused by American leishmaniasis are polyps of the frontal sinuses (ESCOMEL) pedunculated nasal polyps (Mangabeira) cheilitis and paronychia (COSTA)

RABELLO's classification indicates the great clinical variety one can expect in American leishmaniasis. Classifications based on the similarity with other diseases, used by some authors, give a good indication of the differential diagnostic problems. The following terms may serve as examples, lepromatous framboesiform, blastomycotic, chromoblastomycotic, syphiloid, pyodermic, epithelioma-like and sporotrichotic leishmaniasis.

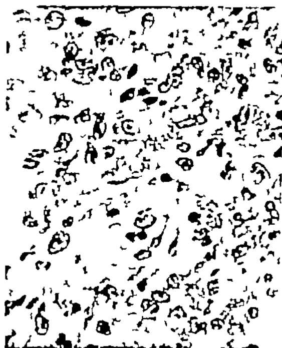
PATHOLOGY

American leishmaniasis presents histologically the picture of a specific infectious granuloma with a rather wide range of reaction.

The fundamental reaction caused by Leishmania braziliensis is reticulo-endothelial proliferation. The organisms do not cause suppuration. As previously mentioned, L. braziliensis is morphologically indistinguishable from L. tropica and also from L. donovani In infections with L. donovani in visceral leishmaniasis where enormous numbers of parasites are present in spleen and liver the endothelial proliferation is in the foreground and no suppurative features are present.

The histological picture of American leishmaniasis, although in some respects similar to the one seen in oriental sore, is less uniform than in the latter Basically there is an infiltrate in the corium or the submucosa with subsequent epidermal and tissue reaction. Thus infiltrate can range from an unspecific accumulation of inflammatory cells, arranged in an uncharacteristic way to formation of tubercles with central caseation and an accumulation of epithelioid cells, giant cells, lymphocytes and plasma cells in the periphery Often there are

foci of epithelioid cells in the upper cutis occasionally with giant cells. The giant cells are sometimes of the Langhans type, sometimes of the foreign body type Bussr calls attention to the large number of nuclei in these cells which show a peripheral arrangement and have thread-like bridges between them. In the central zone of the lesion the infiltrate reaches directly into the epidermis while in the border a small zone of normal connective tissue is seen between focus and epidermis.



340 American leishmaniasis. Leishmaniae within the histiocytes.

Within the infiltrate there is destruction of collagen and elastic tissue. The epidermis itself can be either atrophic from the pressure of the underlying infiltrate, or it can become hyperplastic, corresponding to the papillomatous and verrucous clinical forms Heavy acanthosis predominates

If ulceration occurs the epidermis is missing in the center of the lesion and is replaced by layers of fibrin with polymorphonuclear

leukocytes, erythrocytes and cellular detritus. Underneath lies the inflammatory infiltrate with epithelioid cells and giant cells in addition to lymphocytes and plasma cells. Occasionally Russel bodies can be



341 American leishmaniasis tuberculoid histology
(Fasal & Graber–San Francisco)

observed In the periphery of the ulcer pseudoepitheliomatous hyper plasia of varying degree is seen.

The parasites are present intracellularly in the epithelioid cells (histiocytes macrophages) and in the giant cells occasionally they are also seen free in the tissue They are not observed in blood vessels but occasionally in lymphatics. It is often stated that in American leish-

maniasis the number of parasites present in sections is much smaller than in sections of oriental sore. This is not always the case occasionally one can find numerous parasites in sections from American leishmaniasis. The parasites are not seen regularly in all parts and stages of the lesions While it is usually not difficult to find them in the small accumulations of epithelioid cells and giant cells in the upper and middle corium, their number decreases in the depth and the periphery



342. American leishmaniasis Giant cells.

of the infiltrate and they are also not found in the centers of the tuberculoid nodes These centers consist mainly of histiocytes and are called "clear centers" analogous to similar centers observed in tuberculosis and leprosy where it is also difficult to find the causative organisms in accordance with the law of JADASSOHN and LEWANDOWSKY tuberculoid structures are seen where organisms are locally and not too rapidly destroyed by the immune-biological defense mechanism"

Once ulceration occurs, the organisms can be seen only as long as marked infiltration is present. Later on, especially when there is extensive necrosis, it becomes more and more difficult to find the parasites, even in the borders of the ulcer

In cases with subcutaneous involvement one can find abscess formation. The cavity is surrounded by simple granulation tissue or by tuberculoid nodes with caseation.

The changes seen in the mucosal form are even less uniform than the ones just described for the cutaneous form. The earliest finding is an infiltrate in the submucosa which leads to epithelial changes and to ulceration. Again the tissue reaction can vary from a simple inflammatory process to tuberculoid formations. In a mucosal ulcer the epithelial layer is missing, and is replaced by a false membrane consisting of fibrinous exudate with leukocytes, reminding one of diphtheria. Underneath there is a dense cellular infiltrate consisting of polymorphonuclear leukocytes, histiocytes, plasma cells and fibroblasts. The blood vessels are dilated. The leishmaniae are present in histiocytes in the periphery Tuberculoid structure is rather rare in mucosal lesions. If present, it is found near the borders.

According to KLOTZ and LINDENBERG the findings in mucosal leishmaniasis are as follows

1 Perivascular lymphocytic infiltration of the submucosa.
2. Predominance of plasma cells and endothelial cells.
3 Endothelial nodes around the blood vessels
4 Formation of three types of nodes a endothelial b. necrotic, c. fibrous.
5 Endarteritic changes of the blood vessels with frequent occlusion.
6. Leishmaniae in the endothelial cells in all stages.

These authors feel that the extensive destruction of fibrous tissue and cartilage is apparently not caused by the parasites themselves, but is a result of a progressive local endarteritic process and of the subsequent atrophy and necrosis. Others blame the extensive destruction on the secondary infection usually present, while still others hold toxic products from the parasites responsible. I have not found the endarteritic changes to be a constant feature and do not feel that they are characteristic. Rather they may be due to inflammatory processes from secondary infection.

The further spread of the metastatic mucosal lesions occurs via the lymphatics. In the lymph nodes one finds accumulations of epithelioid cells especially near the sinuses with a plasma cell reaction. Later there can be tubercle-like nodes with caseation necrosis and giant cells and finally fibrous changes.

DIAGNOSIS

The clinical diagnosis of American leishmaniasis is often difficult, as this disease is capable of imitating numerous other conditions. Among the diseases which have to be considered in the differential diagnosis are: Syphilis, yaws, tuberculosis, leprosy, deep mycoses (especially blastomycosis, chromomycosis and sporotrichosis), granuloma inguinale, diphtheria of the skin, pyoderma vegetans, rhinoscleroma, rhinophyma, rhinopharyngitis mutilans, tropical ulcer and myiasis.

It is essential to confirm the clinical diagnosis by laboratory methods. Leishmania braziliensis exists in two forms: the *flagellate leptomonad form*, found in the insect host and in cultures, and the *pure leishmania form*, found in the tissue.

For *direct examination* and for culture the material has to be obtained carefully to avoid contamination with blood and secondary invaders. The lesion either can be scraped with a sharp knife or a pipette can be introduced at the border of the lesion, be it ulcer or nodule, and the tissue fluid aspirated. The latter method is much more apt to give uncontaminated material and is to be preferred to the former. Smears are made and stained like blood slides, preferably with Giemsa. For cultures numerous media can be used, the most universally successful being the N N N medium. BELTRAN recommends adding 1 to 2 ml of sterile saline solution to each culture tube which permits keeping it longer. He also suggests adding a small amount of penicillin to the culture after inoculation to avoid contamination from secondary invaders.

Laboratory animals are susceptible to leishmania braziliensis, as mentioned earlier. The diagnostic value of animal inoculation is limited.

Complement fixation tests and *agglutination tests* are of theoretical interest but have little practical value at present due to technical difficulties.

Xeno-diagnosis has to be reserved for special cases on account of the obvious difficulties connected with a method which depends on the demonstration of parasites in insects fed on suspected lesions.

Histopathological examination is an important diagnostic aid. The parasites can be seen in sections, even when smears fail to reveal them. A piece of tissue can easily be removed and kept for processing at a later date when the facilities are available. This can not be done with material for culture which has to be processed immediately. The histopathological picture alone is not characteristic enough to make a diagnosis; to this end the parasites have to be found.

Extraneous substances and yeastlike formations as well as other organisms can be confused with Leishmania braziliensis by the inexperienced observer. Donovania granulomatis, seen in granuloma inguinale, Histoplasma capsulatum (histoplasmosis), Toxoplasma and the leishmania form of Trypanosoma cruzi can look much alike. As a matter of fact, L. braziliensis and the leishmania form of Trypanosoma cruzi look identical in tissue, both having a kinetoplast and a parabasal body. However, Trypanosoma cruzi affects only parenchymal cells and not histiocytes. Granuloma inguinale shows significant plasma cell accumulations and small abscesses with polymorphonuclear leukocytes. Donovania granulomatis, Histoplasma and Toxoplasma do not have kinetoplast and parabasal body. Histoplasma has a clear capsule and Toxoplasma is always associated with focal necrosis.

In 1923 E. H. WAGENER reported on a *skin reaction* obtained with extracts from L. tropica and infantum in sensitized rabbits. In 1926 MONTENEGRO developed a diagnostic method employing extracts of various strains of L. braziliensis and proved this reaction to be specific for leishmaniasis. BUSS attempted to use the skin test to differentiate the various species of leishmaniae, but came to the conclusion that the skin test, though specific for leishmaniae in general, could not be employed as a means to differentiate one species from another. DOSTROWSKY used a vaccine containing killed parasites for *intradermal tests*, while SAGHER employed a vaccine prepared from washed flagellates.

The *intradermal leishmanin test*, easily carried out, is of great practical value. It indicates past or present infection with Leishmania braziliensis or tropica and it is felt that this test should be used on a much larger

scale (CASAL and GRADOS) Some authors insist that the diagnosis of leishmaniasis of the skin or mucous membranes must be confirmed by *culture* since all other methods including smears and examination of stained sections are not conclusive While it is correct that occasionally it can be difficult to come to a definite conclusion when examining smears and sections for parasites I feel that in these cases additional evidence can help make the diagnosis. A suggestive clinical picture a confirming history parasites in sections of tissue and a positive intradermal test must in my opinion be accepted as sufficient evidence even if cultural confirmation is lacking

THERAPY

The fact that numerous drugs and methods of treatment are recommended for American leishmaniasis makes it obvious that so far no specific therapy is available

Of *local methods* surgical excision cauterization and destruction by electro-surgery are used. Freezing with carbon dioxide snow X ray and Grenz ray therapy also are being employed with beneficial results. Various local applications like antimony ointments as well as sulfonamides and penicillin have not been too successful Local injections of atabrine and also of a 1 % sol of berberinum sulfuricum (from berberis indica) are used.

Among the various *systemic medications* antimony salts occupy a prominent place Tri as well as pentavalent combinations are used and are given intramuscularly and intravenously Emetin, arsenicals (tri and penta valent), Bismuth and iodobismutal of quinine are recommended by various authors Vaccine therapy seems to give promising results but needs further studies and large scale experiments Sulfonamides, penicillin and streptomycin seem to act on secondary invaders, but not on the leishmaniae themselves.

The cutaneous lesions of American leishmaniasis and the mucosal lesions which are simply a continuation of the skin lesions react well to most of the above mentioned drugs and methods. The so-called *metastatic mucosal lesions (espundia according to* ESCOMEL) do not show much effect from all available therapeutic methods

PROPHYLAXIS

Personal prophylaxis comprises active and passive immunization which seems to be effective in preliminary experiments. Further studies are necessary. Protection of individuals from the bite by phlebotomus can be achieved by extermination of the insects, screening of bed rooms, use of insect repellents and similar measures.

Hertig and Fairchild report that control of phlebotomus in two large construction camps in Peru was followed by an almost complete cessation of new cases of cutaneous leishmaniasis. A 5 % solution of D.D.T. in kerosene was used in a concentration of one gallon to 1 000 square feet.

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SOUTH AMERICAN TRYPANOSOMIASIS (CHAGAS' DISEASE)

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DEFINITION

South American trypanosomiasis is a rare infectious non-contagious disease, affecting children and adults and occurring in an acute and a chronic form. It is caused by Trypanosoma cruzi It is also known under the name of *Chagas' disease* after CHAGAS who found Trypanosoma cruzi first in the intestines of a reduviid insect and was able later to demonstrate it in the blood of children suffering from a severe febrile disease

EPIDEMIOLOGY

South American trypanosomiasis is principally seen in Brazil, Argentine and Uruguay and less frequently in Bolivia, Chile Colombia, Costa Rica Guatemala, Guiana Mexico, Panama, Peru, San Salvador and Venezuela

The geographic distribution of the disease in humans does not coincide with the distribution of the insect vector In Ecuador Paraguay a well as in California, Arizona, New Mexico and Texas reduviid bugs infected with Trypanosoma cruzi have been found, but so far no case of South American trypanosomiasis in humans has been reported in these areas

AETIOLOGY

The causative organism is generally called Trypanosoma cruzi, but is also referred to as Schizotrypanum cruzi In the blood of men and in

the vector it appears as a trypanosome, in the tissue it assumes a leishmanial form.

The trypanosome is spindle shaped, 20 micra long, with a kinetoplast near the posterior end (consisting of a blepharoblast and a parabasal body), has an undulating membrane and a free flagellum. The leishmanial forms, found in the tissue, especially in parenchymatous cells are round or oval bodies about 3 micra in diameter They multiply by repeated binary fission until cystlike structures are formed which destroy the infected tissue.

The main vector is one of the reduviid insects, mainly Panstrongylus



343 Chagas disease blood film.

(Triatoma) magistus or infectans. Triatomata are blood suckers and bite on exposed parts of the skin like the face, usually near the eyes or on the lips They are also known as cone-nosed bugs, assassin or kissing bugs. The insects bite during the night, hiding during the day in cracks of poorly constructed, unhygienic huts, stables and in the burrows of rodents. Dogs and cats are naturally infected. In Brazil the armadillo is the natural reservoir in other South American countries the otter and the opossum. All laboratory animals can be infected with Trypanosoma cruzi.

The infection is common only among the poorer classes of natives and severe cases are usually encountered in children under two years of age

He explained the frequently observed oedema as a myxoedematous manifestation caused by the resulting dysfunction of the thyroid gland. However it is believed now that the thyroid involvement if present, is incidental, as it is mainly found in areas in Brazil where goiter is endemic and not at all in Peru and Guatemala where there is no endemic goiter Other manifestations like nervous disorders and mental dullness considered to be symptoms of the chronic form of South American trypanosomiasis may also be due to co-existing thyroid disturbances and unrelated to the disease

So far no skin manifestations have been reported in the chronic or late stage In experimental infection intermittent fever starts after an incubation period of 7 to 14 days and usually lasts for 3 weeks. Trypanosomes can be found in the blood after 6 weeks.

In the acute febrile stage organisms are usually found in the blood, but are seldom demonstrable after the temperature drops. In the acute form they can be found also in the spinal fluid in terminal cases They are hardly ever present in the blood in chronic cases However there are people whose blood contains trypanosomes and who do not exhibit any clinical manifestations of the disease They are considered to have the so-called asymptomatic form of South American trypanosomiasis

PATHOLOGY

The acute phase of South American trypanosomiasis is characterized by necrosis. In chagoma there is necrosis of the epidermis with an inflammatory infiltrate consisting of polymorphonuclear leukocytes and histiocytes in the corium. There is extensive fat necrosis in the subcutis

In the exanthematic eruptions of the acute stage there is a perivascular round cell infiltrate in the corium with some histiocytes. Trypanosoma cruzi in its leishmanial form can be found in histiocytes and fat cells.

The largest number of leishmaniae are always seen in the heart muscle where they can be found in cyst like formations within the muscle fibers.

In the chronic or late stage proliferative processes are the *main* histological feature, which can eventually lead to fibrosis

The differential diagnosis of Trypanosoma cruzi in its leishmanial form from Leishmania braziliensis can be most difficult, as they look identical, both having a kinetoplast and a parabasal body however Trypanosoma cruzi generally affects only parenchymatous cells like cells of the heart muscle, brain, and skeletal muscle, while Leishmania braziliensis and tropica affects histiocytes. Only in the skin manifestations of the acute stage of South American trypanosomiasis are the



345 Chagas disease Leishmania form a Trypanosoma cruzi in heart muscle

organisms seen in histiocytes. Donovania granulomatis, Histoplasma capsulatum and Toxoplasma can look much alike but do not have a parabasal body

DIAGNOSIS

In the acute stage the parasites can be demonstrated in the peripheral blood by examination of fresh or stained blood films, thin or thick.

If this examination should not give the expected result, intraperitoneal inoculation into white rats or guinea pigs should be undertaken. In fresh cases 0.5-0.75 ml citrated blood are sufficient, while in older cases 5-10 ml are necessary.

Other diagdostic methods are

Xenodiagnosis with uninfected reduviid bugs.

Culture of blood on N N N medium or on blood broth.

Muscle or gland biopsy for histopathological examination.

Spinal fluid examination in cases of meningo-encephalitis.

The Machado-Guerreiro reaction is a complement fixation test with a glycerin-water extract of heart and spleen of heavily infected puppies as antigen. It is considered specific by numerous observers. In experimental inoculation it becomes positive within 10 days. It remains positive for many years. A modification by KELSER also is being used as well as precipitin and agglutination tests.

An intradermal test with a "Cruzin" prepared from Trypanosoma cruzi is being used and considered helpful but not absolutely conclusive.

THERAPY

Drugs which are effective in African trypanosomiasis are of no value in South American trypanosomiasis. Bayer 7602 or surfen active *in vitro* in South American trypanosomiasis is dangerous in human beings owing to its toxic properties. Other drugs now being evaluated are M 3024 and 9736 Bayer.

In addition to these newer chemotherapeutics blood transfusions, liver and vitamin B are beneficial as supportive therapy. Penicillin and some of the newer antibiotics do not have any specific action, but may influence the course of the disease to some extent owing to their action on secondary invaders.

PROPHYLAXIS

Proper use of mosquito nets protects from the insect vector. Destruction of infected domestic animals and pets is essential, as well as protection from armadillos and other animal hosts in the construction of living quarters.

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CHAPTER 14

CUTANEOUS AMOEBIASIS

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DEFINITION

Cutaneous amoebiasis is the term applied to the infection of skin with the protozoan parasite *Entamoeba histolytica*. Invariably it is secondary to amoebiasis of other tissues.

HISTORY

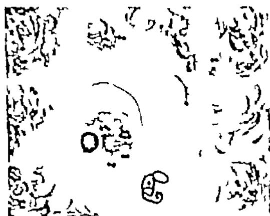
Since the first published record of cutaneous amoebiasis by Nasse (1892) a considerable literature on it has appeared in various parts of the world. Nomi and Frazier (1933) collated records of twenty seven cases in some of which the specific diagnosis is open to question. Although numerous additional case records have since been published there must have been a great many other cases of cutaneous amoebiasis which have not been publicized.

AETIOLOGY

Entamoeba histolytica in nature is primarily a parasite of the human large intestine. The amoeba is the only stage of this organism which parasitizes man; amoebae within the bowel when carried rapidly to the exterior appear in the loose stools in the amoeboid form; when they are passed slowly to the exterior in the faecal stream they become inert and resistant cysts. These cysts, which are voided only in formed stools, are the stage of the parasite infective to others; intestinal amoebiasis is acquired by swallowing them. *E. histolytica* cysts in

nature, are never formed in any tissue or medium other than faecal material actually within the large intestine, and then only if sufficient time elapses for their formation.

The cysts of *E histolytica* in stools can readily be specifically identified by their unmistakable detailed morphology The amoeboid forms of this parasite in stools are identifiable by their appearance, detailed morphology and contents but when found in faeces skill is needed to differentiate them from the morphologically similar amoebae of the allied species *E coli* a harmless commensal parasite Entamoebae found in tissue, however can confidently be identified as *E histolytica*,



346. A vegetative *Entamoeba histolytica* in a piece of slough removed from skin around a liver abscess drainage wound.

because *E. coli* and the other intestinal amoebae are not tissue-invading parasites but live only within the lumen of the large intestine.

An *E. histolytica* infection of the large intestine can spread to other tissues either by direct extension or by embolic carriage in the blood stream. The liver not uncommonly is infected through the portal circulation by the latter means from this organ, as from any focus of amoebic infection, the amoebae may extend, or be conveyed, to further sites by similar means. But without exception, in every case of extra-intestinal amoebiasis in nature, the infection originates in the large intestine

Cutaneous amoebiasis is never an embolic infection it is always due to local extension of the primary intestinal focus of infection or of a secondary focus of infection. This occurs either directly through the tissues, or much more commonly as a result of contact usually prolonged, with a discharge containing active amoebae This discharge may be liquid faecal matter and infection of the perianal or perinaeal skin may occur from an *E histolytica* infection of an intestine which, though ulcerated is anatomically intact. If there is an infected faecal discharge from a wound in the bowel, such as a colostomy opening, the skin surrounding this is liable to be infected with amoebae Alternatively the discharge may be non faecal in character and immediately derive from a secondary and extra intestinal source of amoebic infection, such as a fistula discharging material from an amoebic liver abscess invasion by amoebae of the skin around the sinus may and usually does ensue unless proper measures are taken to forestall it The amoebic skin infection, in either event, is not necessarily limited to the skin it commonly extends to the adjacent deeper tissues as it progresses.

It would be no exaggeration to say that amoebiasis of the skin is due to the neglect or inability of the patient to seek timely advice or else it is due to a failure on the part of his medical advisers to recognise the existence of the causative infection, to appreciate its potentialities, and to treat it properly With adequate knowledge and efficient diagnosis and treatment infection of the skin with *E histolytica* should not occur

SYMPTOMATOLOGY

The appearance of any persisting and spreading skin lesion around a point of continuing discharge of possibly amoeba infected material should at once arouse a suspicion of cutaneous amoebiasis. Although STRAUB (1924) reported a case of cutaneous amoebiasis of the penis following sodomy such brief and casual contamination of skin can but exceptionally result in cutaneous amoebic infection. The areas of skin usually found to be involved are those kept moist by a discharge, by contiguous contaminated skin surfaces or by soiled surgical dressings. Commonly in the recorded cases of cutaneous amoebiasis, the amoebic content of the infecting discharge escaped notice until the cutaneous

lesion became so obtrusive and extensive as to demand further investigation. The whitish necrotic sloughs of cutaneous amoebiasis are insensitive, and the living tissue around them is rarely tender or painful. In a few cases associated with amoeboma formation it has been recorded that the lesions were both painful and extremely tender.

Among those examples of cutaneous amoebiasis which are due to delay by patients in seeking advice perianal and perineal infections, often superimposed on other conditions such as *fistula in ano* or anal fissure, or condylomata, predominate. Excoriation of the buttocks of



347 Cutaneous amoebiasis following operation for liver abscess.
(Touraine and Ménétrier–Paris)

persons debilitated and prostrated by prolonged and severe amoebic dysentery facilitates extension of the amoebic infection into the damaged and soiled skin. Once established in the skin an amoebic infection continues to extend: it shows no tendency to spontaneous healing. A very wide area of skin and adjacent tissue ultimately may be involved before the patient is treated or dies. MANSON BAHR (1939) cites an example of this, in which an infection of the perineum spread to the buttocks and also to the anterior abdominal wall before its specific causation was recognized and suitably treated. In such a case the tissues underlying the skin would be extensively invaded by the

parasites the patient would progressively become more ill and he would die unless properly treated.

Cutaneous and subcutaneous amoebomata on occasions have been mistaken for neoplasms and the patients have accordingly been subjected to major operations. This error has been reported in the literature on several occasions. Firm or hard skin and subcutaneous amoebomata are especially prone to develop in the perianal region, or in other areas of faecally conveyed amoebic infection of the skin



348 Cutaneous amoebic phagedaena of the abdomen.
(Elbert Bamberg)

where the bacterial contamination is varied and prolific. That the tumours show no tendency to break down, or to suppurate freely further suggests a neoplastic origin. GHOSH and MUKHERJI (1950) report a case of suspected squamous-celled carcinoma treated surgically which proved in fact to be a perianal amoeboma: the lesion rapidly resolved and vanished under emetine treatment. FREEMAN, SCHREK and BROWN (1940), HAWE (1946), and KOURI, IRIONDO and

PERAZA (1949), among others, have recorded cases in which malignancy was first suspected in lesions which ultimately proved to be due to cutaneous amoebiasis with amoeboma formation all these cleared rapidly when specific treatment with emetine was given.

PATHOLOGY

The amoeboid forms of *E. histolytica* secrete a cytolytic ferment, hence the specific name. This enzyme produces colliquative necrosis immediately around individual amoebae or colonies of amoebae. All



349 Cutaneous amoebiasis and amoeboma formation at site of colostomy wound.

types of cells are destroyed by it there is no inflammatory response to the parasites, and the necrotic area around colonies of amoebae shades off into histologically normal surrounding tissue, with no specific adventitious cellular demarcation. There is no true pus formation as a result of the amoebic infection but pus will be formed in amoebic lesions when bacterial infection complicates the pathology

Commonly though secondary infection with staphylococci and other prevalent skin contaminants is usual, amoebic infiltration of skin is not at first associated with inflammatory changes of bacterial origin.

The amoebic infection steadily penetrates to the deepest layers of the affected skin and to the underlying tissues. The affected area appears as a greyish or whitish necrotic slough; especially at its periphery enormous numbers of actively motile amoebae will readily be found in it. As already stated, amoebae in such a lesion can with confidence be identified as *E. histolytica*.

An amoebic infection of the bowel which extends extra-intestinally within the abdomen not uncommonly is associated with the formation of hard tumours; these are the result of chronic inflammatory changes due to associated bacterial infection; the tumours are known as amoebic granulomata *(amoebomata)*. Amoeboma formation is unusual in cutaneous amoebic lesions such as those that occur around the discharge wound of an amoebic liver abscess. But it may, and often does, occur in association with amoebiasis of the skin due to infection from a faecal discharge; amoeboma formation is by no means unusual in cutaneous amoebiasis of the perianal region, or around a colostomy wound, where the bacterial contamination is gross and varied.

DIAGNOSIS

Scrapings of the lesions, or pieces of the necrotic sloughs removed with forceps, if moistened with saline and examined microscopically without undue delay will reveal the presence of actively motile amoebae. The amoebae are most numerous in material taken from the periphery, or from the deepermost layers, of the lesions. There can be no reasonable doubt about the identity of amoebae recovered from such sites.

THERAPY

The specific treatment of cutaneous amoebiasis is confined to the use of the alkaloid emetine. Daily doses of one grain of emetine hydrochloride, given subcutaneously or intramuscularly, will sterilize an amoebic infection of the skin with remarkable rapidity and certainty, usually within a very few days. These injections should be continued over a period of twelve days. In addition to sterilizing the skin infection they will also eradicate any other extra-intestinal focus of amoebic infection, including that from which the skin lesion imme-

diately arose. Very rarely it may be necessary to repeat the course.

Unfortunately emetine treatment alone does not sterilize the primary bowel infection. Sterilization of this must be achieved or further secondary infections with amoebae are liable to take place. After the completion of the emetine treatment therefore the eradication of the intestinal infection must be undertaken. The drugs now employed to achieve this end include emetine-bismuth-iodide (E.B.I.), an arsenical such as stovarsol, one of the iodo-hydroxyquinoline compounds such



350 Peri-anal vegetative amoebiasis of 35 days duration.
(Ngal and Fraeger-Presse Med 1939)

as chiniofon, which is given as a retention enema, and, possibly either terramycin or aureomycin. The choice and the modes of administration of these compounds vary with individual practitioners it is usual to give a number of them in concert over a period of two or three weeks to ensure complete parasitic cure of the primary bowel infection.

The prevention of cutaneous amoebiasis is more important than its cure. When surgical drainage of any amoebic abscess is undertaken emetine should *always* be given concurrently to sterilize the abscess of its parasites. If this is done and if the discharge from the sinus while it

persists is regularly examined to ensure that it contains no parasites, cutaneous amoebiasis following surgical intervention—its commonest cause in the more advanced countries—should not be seen



351 Erythemato-squamous condition with furunculoid lesions or dermatitis desquamativo-pustulosa amoebica.

(Engman and Heithaus—Presse Méd 1939)

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DISEASES DUE TO BACTERIA

ULCERATION IN THE TROPICS

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INTRODUCTION

A variety of ulcers is found in tropical countries. Some, such as oriental sore (leishmaniasis), desert sore, ulcus tropicum, coral ulcer blastomycetic ulcer and ulcers due to yaws are seen only in the tropics or in persons who have recently been in such parts others, such as amoebic ulcers, and those associated with sickle and target cell anaemia are more common in the tropics but may be found elsewhere whereas some, such as ulcus cruris and syphilitic ulcer have a worldwide distribution.

Much confusion of terminology has resulted from the application of words such as oriental and tropical to any ulcers which may be seen in the hotter parts of the world. Moreover many synonyms are in use chiefly based on place-names, further adding to the confusion.

In this chapter we shall consider *ulcus phagedaenicum tropicum desert sore* and *coral ulcer* Details of oriental sore (leishmaniasis) will be found in chapters 11 and 12. See also Noma Madagascar chapter 17

ULCUS PHAGEDAENICUM TROPICUM

DEFINITION

Tropical ulcer is a painful, rapidly spreading (*i.e.* phagedaenic) ulcer often solitary and usually affecting the lower limbs. The base is sloughing the margin undermined sometimes raised and irregular and there

may be local oedema. In depth the ulcer may reach the periosteum, the fascial covering of muscles or the tendon sheaths. Synonyms are *Naga sore*, *Annam ulcer*, *Cochin sore*, *Aden ulcer*, *Yemen ulcer*, *Malabar ulcer*, which are also used to signify other ulcers, particularly those of leishmaniasis. (See also *trench mouth*.)

EPIDEMIOLOGY

This condition is found in most countries with a hot, damp climate, and particularly in the jungle. A high seasonal rainfall and marshy



352. Plaut-Vincent's fuso-spirillar symbiosis. Said to be the cause of ulcus tropicum, but not always found and sometimes only one form of both organisms.

land seem especially favourable, and in such a locality it may reach epidemic proportions. James, Manson-Bahr, Patterson, Simons and others have described epidemics in Melanesia, Algeria, Assam, and among prisoners of war in Sumatra. Usually it is endemic and sporadic, being found in many tropical countries: Assam, Cochin China, Malaya, Sumatra, Mozambique, Kenya, Uganda, British Somaliland, Melanesia (especially the Solomon Islands and New Guinea) and parts of Central and South America. Less commonly it may be found in drier places as in Aden, and one of us has seen the condition in Iran.

According to EARLE (1939) and HARE (1948) the affection occurs especially during the dry monsoon, when there is little rain. MANSON BAHR found it to be frequent in and around rubber plantations this was also evident in the P O W camps in Sumatra.



333 Tropical phagedaenic ulcer at its predilection place Usually round, margin undermined, sloughing base.

AETIOLOGY

Ulcus tropicum is a disease of labourers and carriers especially the bare footed and of soldiers on campaign. It is rare among women and children, but is said to be common among cripples, orphans old people and others incapable of earning an adequate subsistence wage.

That tropical ulcer should be attributed to poor nutrition of the patient cannot be accepted without reserve. *Malnutrition* might affect

the development of the ulcer without necessarily being its cause. Thus in tuberculosis malnutrition may be a predisposing factor but KOCH's bacillus is the causative agent. Diet according to ROY (1939) plays no part in the aetiology of these ulcers. HART wrote in 1948 " ... it can hardly be said that the evidence in favour of regarding tropical ulcer as a deficiency disease is conclusive. It seems far more probable that the poorer classes, whose habits render them liable to exposure to



354. Tropical ulcers.
(Orig. G. C. sta-Bele Herbeek)

infection and therefore to dietary deficiencies, will be noted as a rule in populations among which tropical ulcers occur." According to HARE tropical ulcers are found more often among hard working healthy men than among anaemic malaria patients. On the other hand there is much sound evidence that malnutrition plays an essential part in the aetiology. LOEWENTHAL (1950) found in Uganda that tropical ulcer never affects those who take milk and meat and that the incidence

in vegetarians in certain African tribes is high, whereas other branches of the tribe who eat fish are entirely free. Earlier evidence was provided by CHARTERS (1943) from the incidence of tropical ulcer among East African and Somali troops. Both groups were living under identical climatic and other conditions except for a difference in diet. Tropical ulcer was confined to the Somali battalions in which the incidence was high. The main dissimilarity between their diet and that of the East Africans was a deficiency of vitamin A, riboflavine and calcium. Another Somali unit whose diet was not deficient in this way was not affected by ulcer but Abyssinians in East African units, who refused the East African rations, developed typical tropical ulcers. Therapeutic tests with vitamins and calcium confirmed the view that malnutrition was a cause. BERRY who studied the incidence of tropical ulcer in Nyasaland found dietetic factors in the aetiology not the most important, yet faults in the diet were commonly found.

A *seasonal incidence* of ulcus tropicum was noted by LICHTMAN (1947) and related to shortage of amino acids during the periods that maize was the staple diet in winter when cattle were killed and eaten, the trouble disappeared. A diminution in the plasma level of vitamin C in patients with ulcus tropicum was found by ADAMSON (1949), and POINDEXTER (1950) considers that a diet deficient in proteins and vitamins is a factor in the chronicity of the ulcers.

It would seem that malnutrition is an important, if not the only cause of these ulcers. Probably the deficiency state relates to lack of more than one factor

As a precipitating cause of tropical ulcer *trauma* seems important, whether from cuts, pricks, insect or animal bites or poisonous plants ADAMSON (1949) found trauma to be a factor in 98.5 per cent. of a series of tropical ulcers.

Secondary infection of the injured skin occurs by contact with earth, flies or various objects (even rattan baskets) At first a mixed bacteriological flora is found, with haemolytic streptococci and staphylococci, and sometimes Bacillus proteus diphtheria and diphtheroid bacilli, and Candida albicans. Usually the Gram-negative Fusobacterium plauti vincenti (or Bacillus hastilis SEITZ) appears together with Borrelia vincenti which can be stained with methylene blue (*cf* Giemsa). Both are obligate anaerobes and appear to exist in symbiosis. PROWA

ZEK in 1907 named this spirochaete after SCHAUDINN though it had previously in 1905 been named by BLANCHARD after VINCENT (The term [illegible] chaudinni may give rise to confusion with Sp. pallida). Both BLA[illegible]n and PROWAZEK thought this spirochaete to be the cause of tr[illegible]l ulcers and it is certainly often to be found in them. POINDEXTER [illegible]50) investigating these ulcers in Liberia found, during the wet [illegible]n, staphylococci and VINCENT's organisms in symbiosis so[illegible]s only spirilla were present. During the dry season more



355. "Kissing" tropical ulcers with strong vegetative base
(*Sagher, Jerusalem*)

fusiform bacilli were seen, sometimes without spirilla, and frequently diphtheria bacilli.

How does infection with VINCENT's organisms in symbiosis arise? According to APOSTOLIDES (1922) and CLEMENTS (1936) it is from the mouth of the patient or of some other person, according to MARSH and WILSON (1945) from ordinary dirty skin. PANJA however did not find these organisms in the mouths of his patients, and EARLE observed that while VINCENT's symbiosis is of frequent occurrence in North Peru, tropical ulcer is unknown there (quoted from HARE).

JAMES, TUNNICLIFF, SMITH and others assume that the fusiform bacillus is a stage in the development of the spirillum and certainly in cultures the bacilli appear first and the spirilla later. MARSH and WIL-

SON (1945) believed that the disappearance of these organisms in symbiosis from an ulcer is a sign of recovery

Inoculation experiments have not proved conclusively that VINCENT's organisms are the cause of these ulcers. On intact skin such experiments usually fail, but if the skin be abraded or if the infective material be injected subcutaneously ulceration may follow but only if both partners in the symbiosis are used (SMITH PATERSON) STRONG describes the accidental infection of a nurse who cut herself with a knife



356. Tropical ulcer Infection of a scratch wound.
(Orr G Carta—Bela Horizonte)

used to excise a tropical ulcer although the wound was immediately treated with lysol solution. On the other hand, JAMES assumes that infection may follow the mere application of pus from an ulcer on to the skin.

Debilitating disease has been thought by some workers to be an aetiological factor of importance malaria and scurvy by APOSTOLIDES (1922) alcoholism and dysentery by SOPRANO (1914) syphilis by MENDELSON (1921) and ancylostomiasis by HUGHES (1931)

In conclusion, it would seem that a variety of factors are important in the aetiology of tropical ulcer MARSH and WILSON (1945) summed up the aetiology in an "F-quartet" *Filth-Food-Friction-Fusospirillosis*

The incubation period of tropical ulcer is between 2 and 4 days according to COSTA but PAMPANA found it to be 29 days.

SYMPTOMATOLOGY

Ulcus tropicum, often starting with a scratch or as a vesicle, soon comes to have a well-demarcated margin, usually but not always undermined. Sometimes the edge is raised or even callous and is often irregular. The ulcer is foetid with a greyish-yellow purulent and sloughing base which may be limited by the periosteum, the fascia over muscles or tendon sheaths. In 10 per cent., according to ADAMSON (1949) there is periostitis or necrosis of bone and some



357 Tropical ulcer on vaccina.
(Snijders Amsterdam)

times tendons nerves and vessels may be destroyed (ROY 1939). One of us in Sumatra did not find affection of bone in more than 2 %.
Regional lymphatic swelling is usually absent.

Walking and standing are often painful be... the ulcers are commonly present on the legs. This was so in ... cent. of POIN-DEXTER's patients an... 8 per cent. the ulce... olitary. They are rarely seen on th...

A characteristic of ... hagedaenic ulcer ... it owes its name, is *rapid periphe*... There is increas... in the direction of gravit... walking patien... all bulge in the round out... lcer in the di...

and in the recumbent patient in the direction of the calf[1] When the ulcer spreads only in depth it is called "*terebrant*" The surrounding skin looks quite healthy if it is slightly inflamed it will often be found also to be undermined to the extent of the inflamed area. After healing, the ulcer leaves a radiating scar *Keloid* is a rare complication, even in the coloured races. VELDHUYZEN VAN ZANTEN (1948) noted that



358 Fatal tropical ulcer

(*Rodhain–Ameers*)

prolonged tropical ulceration in growing children may cause lengthening of the affected leg even though the bone underneath is almost never affected.

The course of the ulcers is variable. Usually they are chronic and SUTTON states that in well-fed labourers the average duration of an ulcer the size of half-a-crown is about three months The average duration of ulcers (large and small) is 141 days according to MANSON-BAHR. In certain rare cases the phagedaenic character of the ulcer may be excessive and the course disastrous. *Ulcus tropicum gallopans* (also called pyoderma gangraenosum BRUNSTING, GOECKERMAN, O LEARY) races along in or under the skin, and assumes such dimensions that nothing but timely amputation can save the patient. In this

[1] This *gros orteil phenomenon* (SIMONS) should not be confused with *gravitational ulcer* (DICKSON WRIGHT) which is often called varicose ulcer (See also ANONYMOUS Brit. Med. Journ., 1949)

condition the skin of the lower leg and over the knee and tibia is discoloured and blue and more or less translucent owing to the serous exudate beneath. There is widespread epidermolysis: the epidermis over the whole of the lower leg can be painlessly torn away when almost clear fluid escapes. The patient is in an euphoric state and dies within three days in this condition, without any clouding of consciousness until the last. When the lymphatic glands in the groins have become swollen it is usually too late even for amputation. (See also Meleney's ulcer in Chapter 24).



359 Biopsy from border of tropical ulcer. Note inter- and intra-cellular oedema.

PATHOLOGY

Histologically one finds acantholysis, or even total absence of the epidermis; lymphoid and plasma cells in the cutis with necrosis. The edges of the ulcer may show a pseudo-carcinomatous structure. Sometimes there is pronounced oedema of the epidermis at the edge of the ulcer.

DIAGNOSIS

Ulcus cruris (whether varicose or post thrombotic) is limited to the lower third of the leg and is usually close to one or other malleolus. Oedema, varicose veins and other signs of chronic venous insuffi-

ciency are always present. Tropical ulcer while found on the leg in 77 per cent of patients (POINDEXTER, 1950) and often on the lower third, is frequently situated over the tibia. However, ulcus cruris in the tropics may become phagedaenic and take on the character of tropical ulcer making their differentiation difficult and indeed artificial.

Tertiary syphilitic ulcers which are more common on the thighs and near the knees, are usually multiple, grouped in arcs or circles, with areas of scarring They have a punched-out appearance There



360. Pseudo-carcinomatous histology in border of tropical ulcer

is a rare phagedaenic form of tertiary syphilis called phagédénisme géométrique" Other stigmata of syphilis may be found and the Wassermann reaction is usually positive Potassium iodide taken by mouth results in rapid healing

Desert sore should give no difficulty in the differential diagnosis as it is a shallow ecthymatous ulcer usually multiple, present on any exposed surface and not particularly on the legs. Unlike tropical ulcer which is associated with moist climates, desert sore is usually seen in the drier tropical countries.

Tropicaloid ulcer (CASTELLANI) may give some difficulty in the differential diagnosis with tropical ulcer and desert sores. It is given full reference in the next chapter

Oriental sore (leishmaniasis) may be single or multiple. It is common on the face and arms and in the countries where it is found the native children are often affected. On scraping the margin of the ulcer leishmania tropica can usually be demonstrated.



361 Melanotic ulcer initially taken for a tropical ulcer in an Indonesian woman. *(Oomen–Vaessen)*

THERAPY

In the prophylaxis of tropical ulcer the prevention of trauma is important. ROY (1939) advised the wearing of puttees to prevent cuts and abrasions of the legs. Apparently the incidence of these ulcers can be greatly decreased by this simple measure. The importance of diet in the prevention of these ulcers is stressed by LOEWENTHAL (1950) and CHARTERS (1943) found carotene substances useful in this respect.

Rest is necessary in the treatment of these ulcers. Probably rest in bed is required and if there is oedema of the affected limb the foot of the bed should be raised about 20–30 cm.

Local Treatment Every practitioner in the tropics has his own particular method of treatment of these ulcers. Some improvement usually follows, whenever interest is taken in their treatment, whether

iodoform, alasphine or saline is applied, or some antibiotic such as penicillin, sulphonamide or tyrothrycin.

With penicillin or sulphonamide used locally there is danger of sensitization of the surrounding skin, even when it is protected by bland ointments. Many examples of sulphonamide sensitivity were seen in World War II following the local use of sulphonamides (or penicillin powder which usually contains a large proportion of sulphonamide) for ulcers or impetigo. If such substances are used it should



362. Punched out non-phagedaenic tertiary syphilitic ulcer responding to arsenical therapy



363. Phagedaenic tropical ulcer with undermined borders not responding to arsenical treatment. The tropical ulcer which responds to arsenical therapy is in fact yaws or syphilis.

be for less than five days as during this period sensitization is not likely to occur.[1]

As POINDEXTER (1950) has pointed out, the local injection of diphtheria antitoxin is indicated if diphtheria bacilli are found in the ulcer. It is usually wise to give the antitoxin intramuscularly as well, to neutralize any toxin that may have been absorbed from the ulcer.

Active treatment with caustics is sometimes advised. After protection

[1] O'BRIEN considers the most satisfactory treatment for acute and subacute tropical ulcers is by occlusive plaster treatment combined with parenteral penicillin and skin grafting.

of the surrounding skin by zinc paste the ulcer is touched with pure liquid phenol, or the callous edge of the ulcer is removed by curettage. This is sometimes known as "*anfrischen*" (*i.e.* freshening up") of the ulcer margin and is employed when cicatrization takes place too early.

As the treatment of tropical ulcers is lengthy the surrounding skin may become irritated setting up dermatitis and possibly pyoderma. Severe dermatitis may occur during treatment of the ulcer with phenol if drops of the liquid come into contact with the skin.

It is advisable, therefore, and sometimes necessary to apply zinc



364 Pseudo-tropical ulcer on the foot in which treponema pertenue was found. Probably a hybrid with tropical ulcer although Vincent's symbiosis was not found.

(Mars–Carugen)

oil, or fatty powder to the surrounding skin. The addition of 5–10 per cent. sulphur praecipitatum to the ointment or powder will also prevent pyogenic infection, the appearance of which is marked by purulent bullae pustules folliculitis or impetigo.

Once there is infection of the surrounding skin it will require a "concours des pommades" (an ointment match") in which one must distinguish between events in the wound and those around it. The surrounding skin is cleansed daily with non-irritating disinfectants and any crusts are removed or bullae opened. It is then smeared with the sulphur ointment or painted with a 2 per cent. aqueous solution of gentian violet.

The value of *internal therapy* is disputed. Certainly if the patient's diet has been deficient vitamin supplements are indicated. The im-



365 Gangraneous pyoderma. Note irregular border
(Sagher–Jerusalem)



366. Tropical phagedaenic ulcer with irregular borders.
(Dostrovsky–Jerusalem)

portance of an adequate intake of vitamin C in relation to wound healing is well established and large doses should be given, though ADAMSON (1949) found it ineffective The work of CHARTERS (1943)

and others suggests that vitamin A or carotene and riboflavin are helpful. Good results are claimed by LOEWENTHAL (1950) from daily intravenous injections of calcium chloride (10 ml of a 10 per cent. solution). He found that the ulcers become less offensive and that the necrotic tissue is shed more rapidly. Some debilitated patients require intravenous infusions with plasma.

Organic arsenic compounds or bismuth given parenterally and the sulphonamides given by mouth seem ineffective. Antibiotics such as penicillin, streptomycin, chloromycetin (chloramphenicol) or aureomycin may be used with benefit but only if the bacterial flora is first determined and the sensitivity of the organisms to the various antibiotics demonstrated. Penicillin, so often used indiscriminately, is disappointing in the treatment of these ulcers, as might be expected.

DESERT SORE

DEFINITION

Desert sore is a skin eruption, impetiginous or ecthymatous in type, consisting of single or multiple erosions or shallow ulcers, which exude pus and are usually covered with crusts. It affects mainly the exposed parts, tends to extend locally and is slow to heal. If secondarily infected with the Corynebacterium diphtheriae the ulcer is deeper, with a punched-out appearance and a dark, tough scab.

Synonyms are: *Veldt Sore, Natal Sore, Septic Sore, Gifsweer, Brandsweer, Barcoo Rot*[1], *dermatitis cupoliformis*. (See chapter 16.)

EPIDEMIOLOGY

Desert sore is a disease of hot, dry areas and has been observed in desert or mountainous country in the tropics and sub-tropics in Queensland, N. Australia, Afghanistan, India, Iran, Iraq, Syria, Palestine, Egypt, Libya, the Sudan, Italian East Africa, South Africa and Gallipoli.

AETIOLOGY

These sores occur much more commonly in men than in women and more in the fair-skinned and red-headed than in the dark-complexioned. It is uncommon in the natives of the countries in which it is found.

[1] By *jungle rot* we understand a secondarily infected contact dermatitis or *infectious eczematoid dermatitis*.

There is a *seasonal incidence* in N Australia. In the Western Desert the sores were more common in the summer according to HENDERSON (1943) and in the autumn according to GEAR (1944) However in Iraq they were found equally throughout the year (ANNING 1946)

BETTLEY (1943) considered that *contagion* played an important part and that the condition was related to impetigo (ecthyma). He found in the Western Desert, that 60 per cent. of his patients with desert



367 Ulcus phagedaenicum pyogenicum due to haemolytic streptococci, seen in Holland

sore also suffered from impetigo No evidence of contagion could be found in the series investigated by ANNING.

There is considerable difference of opinion as to the importance of *malnutrition* in the aetiology of desert sore. BETTLEY (1943) and GEAR (1944) believed that it played no part The History of the Great War (1924), on the other hand, stated in reference to veldt sore "It was found that the slightest scratch quickly developed into an intractable ulcer which, in spite of all treatment, would last for months and nothing seemed to do any good except to send the patient down the

line to Egypt when, with fresh food and vegetables and ordinary simple dressing the sores quickly healed." MOLESWORTH (1937) was convinced of the importance of diet in Barcoo rot and pointed out that it affected men living in the arid parts of Central Australia where fresh vegetables and fruit are unprocurable and where the diet consists chiefly of salted meat and tinned food. He also noted the improvement when there was a change to fresh food. RAPPORT (1942) agreed that lack of green vegetables was a cause, and ANNING (1946) produced evidence based on consideration of the dietary intake on vitamin-C excretion tests and on the results of therapy with vitamin supplements which suggested that malnutrition was a factor in the aetiology of desert sore.

Trauma is important in the cause of these sores. Abrasions, insect bites, burns and friction blisters are often the precursors of desert sores. They occur more commonly in individuals exposed to injury and affect those parts of the skin liable to trauma – the wrists and hands, forearms, knees and anterior aspects of the legs.

It seems probable that desert sores are the result of trauma affecting skin whose resistance to infection is lowered and whose capacity to heal normally is reduced by malnutrition. Infection seems to be a secondary process but one which may delay healing.

The organisms found in the sores are usually the normal inhabitants of the skin: staphylococci, non-haemolytic streptococci, sarcinae and diphtheroid bacilli. As with other organisms infection with C. diphtheriae is a secondary affair and this bacillus does not seem to affect intact skin. It is certainly not an essential cause of desert sore and many of these sores are never infected by it. *Cutaneous diphtheria usually occurs when faucial diphtheria and carriers are present in the same community and several parallel outbreaks have been reported* (MELCHIOR, CAMERON and Muir). Thus, in the Sinai desert and in Mesopotamia in World War I and in Palestine and Iran in the second World War outbreaks of diphtheritic sores occurred usually when faucial diphtheria appeared, simple desert sores having been present for some time previously. It must be emphasised, however, that diphtheritic sores do not occur during every outbreak of faucial diphtheria, but probably only under conditions when desert sore or some other chronic skin lesion is present.

SYMPTOMATOLOGY

Onset Delayed healing of the primary traumatic lesion is usually observed and the surrounding skin becomes reddened. If the lesion occurs at the site of an abrasion, the latter suppurates, if following an insect bite a pustule appears if at the site of a traumatic blister this becomes filled with pus, and if following a burn the lesion varies according to the degree of burning Thus a blister becomes purulent or a third degree burn fails to heal, the raw surface discharging pus.

Secondary vesicles are usually pinhead in size when first seen. They rapidly increase and within a few hours are 3 to 6 mm in diameter During this period they become pustular and are surrounded by a zone of erythema. The pustules usually burst in 1 to 3 days These secondary lesions may occur a few inches from the original lesion or on some distant part of the body

Ulcer Stage The lesions, whether following an abrasion, burn, bite or blister or occurring as secondary pustules become similar in appearance after about 5 days. A shallow suppurating ulcer with a flat base covered with yellow or greyish debris, and a slightly raised margin surrounded by a zone of erythema, is seen The ulcer usually increases in size up to 25 or even 50 mm diam. The margin of the ulcer can be seen to be undermined in the active stage, and pus, thin and yellow or greyish, can be pressed from under it. In untreated ulcers there appears to be a natural tendency to heal, but this is usually slow and it may be a month or more before the margin becomes flattened and epithelialization commences

If no dressing is applied, a crust of dried secretion appears over the ulcer in one or two weeks and the lesion takes on an ecthymatous or less frequently an impetiginous appearance. The crust is thick, the size of the ulcer and increases with the latter It is firmly attached to the ulcer and pressure on it during the active stage will result in the appearance of pus at the margin. When healing starts the surrounding erythema fades and the margin of the crust becomes loose, when complete the crust drops away leaving a scaly or a smooth scar The scar is thin and often wrinkled.

The patient does not usually complain of ill-health, though he may say that whereas he "used to have good healing flesh, cuts now take a long time to heal." Desert sore in the acute inflammatory spreading

line to Egypt when, with fresh food and vegetables and ordinary simple dressing the sores quickly healed." MOLESWORTH (1937) was convinced of the importance of diet in Barcoo rot and pointed out that it affected men living in the arid parts of Central Australia where fresh vegetables and fruit are unprocurable and where the diet consists chiefly of salted meat and tinned food. He also noted the improvement when there was a change to fresh food. RAPPORT (1942) agreed that lack of green vegetables was a cause and ANNING (1946) produced evidence based on consideration of the dietary intake on vitamin-C excretion tests and on the results of therapy with vitamin supplements which suggested that malnutrition was a factor in the aetiology of desert sore.

Trauma is important in the cause of these sores Abrasions insect bites, burns and friction blisters are often the precursors of desert sores They occur more commonly in individuals exposed to injury and affect those parts of the skin liable to trauma – the wrists and hands forearms knees and anterior aspects of the legs.

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General Treatment Vitamins A and C should be given and a diet containing fresh meat, fruit and vegetables is important. It has been shown that the healing time can be significantly reduced in this way (ANNING 1946)

CORAL ULCER

PRESTON (1950) has described a form of ulceration resulting from contact with living coral reefs. It is well known among the fisherman and pearl divers of the western seaboard of the Persian Gulf and occurs among the fishermen of Ceylon, on the Great Barrier Reef and in Japanese pearl divers working near Thursday Island. PRESTON's patients were affected while in the Qatar Peninsula in the Persian Gulf

According to PRESTON the patient first complains of lacerations of the feet, legs, or hands after contact with living coral reefs. In some cases the lacerations may pass unnoticed or be so minute as to escape attention, or may even be absent. Some 12 to 24 hours later there is pain in the injured area and a spreading area of cellulitis appears around the wound. The course is slow and painful and a deep ulcer appears with *lymphangitis* and *enlargement of the local lymphatic glands* The patient is often unable to walk for weeks or months after the injury and the course is punctuated by sudden relapses when the condition flares up again without warning

The cause is the entry of silica headed darts from the coral into lacerations sustained through contact with the calcareous skeleton of the colony or into normal skin. A toxic fluid is released from the darts and these themselves provoke a foreign-body reaction. Ulceration and secondary infection follow

Prevention treatment should aim at the protection of the feet by special footwear A nutritional deficiency is thought to play no part. Local treatment by curettage of the ulcer and magnesium sulphate and glycerine paste dressings is useful. Secondary infection, usually with Staphylococcus albus, may be controlled by one of the sulphonamide drugs taken by mouth or by intramuscular penicillin.

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CHAPTER 16

TROPICALOID ULCER OR MYCETOID DESERT SORE

ALDO CASTELLANI

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DEFINITION

A contagious ulcer usually superficial, caused by *Micrococcus (Coccobacillus) mycetoides* Castellani 1942. Synonyms are *Superficial Tropical Ulcer Mycetoid Desert Sore Sand Sore Properts Marmarica ulcer Oasis ulcer" Ulcera che dura (Lasting Ulcer) Castellani's ulcer* See also page 428

HISTORY

Until recently this ulcer was confused with true Tropical ulcer (Ulcus tropicum) by some observers and with Veldt Sore (Ulcus Veldis) by others Castellani s investigation in Libya (1940—42) demonstrated that the condition is a disease of its own, separate aetiologically and clinically from both ulcus tropicum and ulcus veldis.

EPIDEMIOLOGY

The ulcer is endemic in North Africa being common in Libya and Cyrenaica where during World War II it took in 1941—42 an epi demic character among the troops of the various fighting nations. Cases occur in many other parts of the Subtropics and Tropics and also in the temperate zones, cases having been recorded in Italy from the Abruzzi and the Pontine regions (Castellani Servino) and in Spain and Portugal (Castellani).

Climatic and seasonal conditions appear to have some importance. In Libya, in Cyrenaica and in Italy the ulcer is more common in the summer months than in winter In Libya the cases are much more common in the plains than in the hills although the Libyan hills (Garian hills) are of very low altitude.



368 Natural tropicaloid ulcer

AETIOLOGY

In films made from the contents of the initial vesicle small coccoid or coccobacillary organisms are seen, which are Gram-negative. They are at times arranged in couples

If tubes of ordinary agar prepared with the usual agar obtainable in Libya and Italy are inoculated direct from the lesions, only a very scanty growth takes place or none at all. If agar of the same origin is used with the addition of trypsin 1 per cent. a fairly good growth is

obtainable the colonies are at first very delicate, dew-drop like, later opaque, greyish or whitish, somewhat streptococcus-like. The microscopical examination of the colonies shows that they consist of coccoid or coccobacillary organisms, which are easily stained by the usual aniline dyes and are Gram-negative. The coccoid forms usually pre



369 Tropicaloid or mycetoid ulcer experimentally produced by inoculation of micrococcus mycetoides.

dominate. Sub-cultures can easily be made on trypsin agar and also on ordinary Italian plain agar, although on the latter the growth is very scanty and may at times be absent. Sub-cultures can be made also in liquid media, broth and peptone water and in this way the fermentative reactions of the organism can be investigated. In liquid media the organism may grow in small groups or in couples or in short chains. The coccal forms usually have a diameter of 0.6 to 1 micron, hand the rod like forms are about 0.6 to 2 microns and more in length

and about 0.3 to 0.6 micron in breadth. When recently isolated the organism grown on the media mentioned is Gram-negative.

Pigment —The growth on agar and 2 per cent glucose agar prepared with American Difco ingredients is much more abundant, and a very interesting feature is that after twenty four to thirty-six hours in the incubator at 35 to 37 C, and also at room temperature after a little longer time, the growth takes on a distinct yellowish tinge which later becomes a well marked yellow pigmentation. The pigment does



370 S perficial type of tropicaloid ulcer

not diffuse in the medium. The yellow pigmentation on American Difco glucose agar is constant. It was suggested that possibly other bacteria which produce *non-pigmented* colonies on media prepared with ordinary Italian agar might develop a pigmentation on American Difco glucose agar but it was found that none of the streptococci, shigellae and escherichiae investigated did so. In Difco glucose agar the coccobacillary and bacillary forms predominate and the organism may become at times partially or completely Gram-positive, phases of

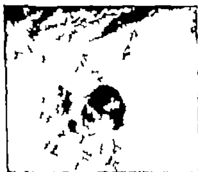
Gram-positivity alternating irregularly with phases of Gram-negativity

Coagulated serum and gelatin.—Coagulated serum and gelatin are not liquefied.

Fermentative reactions.—The organism does not produce gas in any carbohydrate or other carbon compound tried: it produces acidity in glucose and levulose and usually in several other carbohydrates. Mannitol is as a rule negative.

Haemolysis.—This organism is often capable of producing haemolysis.

Pathogenic action on laboratory animals.—The organism has appar



371. Experimentally produced tropicaloid ulcer

ently no pathogenic action on guinea-pigs, rabbits or white rats when inoculated subcutaneously or intraperitoneally.

Classification of the organism.—The exact classification of the organism is difficult especially as while it is present in the lesions as a Gram-negative coccus or a small coccobacillus, in cultures it may take, after some transplantations, a definitely coccobacillary and bacillary form and become partially or totally Gram-positive for some periods of time. For the time being it is probably best to maintain CASTELLANI's nomenclature of *Micrococcus (Coccobacillus) mycetoides*.

Owing chiefly to the appearance of the colonies on Italian agar CASTELLANI was at first inclined to place the organism in the genus *Streptococcus*, sensu lato, but he soon became convinced that this was not correct for the following reasons: (1) The organism in the lesions and when recently isolated and grown on Italian

Reproduction of the ulcer by auto-inoculation and hetero-inoculation.— The ulcer is easily auto-inoculable in the person affected, and is also easily inoculable from the sufferer to healthy individuals. The same technique is used as when carrying out experimental inoculations with cultures. Instead of the culture, a loopful of the contents of the initial



372. Ten days cultures of micrococcus mycetoides on Italian, Difco and Difcodextrose-agar.

vesicle or bulla or some scrapings from the fundus of the ulcer is applied to the scarified zone An ulcer develops identical with the original one

Attempts to reproduce the ulcer with micro-organisms of the associated flora.—As stated, in old open ulcers an abundant associated flora may be present, consisting chiefly of staphylococci and diphtheroid

bacilli Inoculation of cultures of these various organisms including the diphtheroid bacilli never reproduces the typical ulcer but merely causes small inflammatory superficial crusty lesions with no specific characters which usually disappear completely within two to three weeks

Immunity —Natural immunity does not appear to exist. Acquired immunity seems to be very slight or absent, as it is quite easy to inoculate experimentally with the ulcer individuals who have been suffering in the past or are actually suffering from it.

Hypersensitivity —The person affected with the ulcer becomes hypersensitive to the causative organism. The intradermic injection of 0 1 ml of an emulsion of the organism in saline (killed by heat or by addition of ½ per cent. carbolic acid) causes the immediate appearance of a pomphus which after two to three minutes becomes surrounded by a large zone of erythema, which is usually very pruriginous. Ten to fifteen minutes later the erythematous zone begins to become infiltrated and then pruritus ceases. The infiltration lasts for two to three days and then a nodule remains which lasts three to four weeks and after resolution leaves a small hyperpigmented spot which remains for five to six months or longer

The injection of filtered cultures and filtered emulsions produces no reaction

SYMPTOMATOLOGY

The condition is seldom seen in its earliest stage. In such cases one usually notes a superficial flattened large vesicle or bulla as a rule non-follicular which may be surrounded by an inflammatory halo. Within 3 to 4 days from the onset the vesicle or bulla ruptures and a destructive process begins resulting in the formation of a superficial ulcer, which has a tendency to extend in surface rather than in depth.

In a typical fairly advanced case one sees in the lower two thirds of the leg one or two or three, occasionally four (very seldom more) ulcers which may be open or covered by crusts Each ulcer is roundish or ovaloid, rather superficial and the maximum diameter varies between 1 cm and 4 cm or more The margins are not sensibly raised or infiltrated and they are not usually undermined they may show minute indentations. The floor is red, at times covered by a film of pus, at

times granulating occasionally the fundus is covered here and there by small fibrinous pseudo-membranes. The ulcer is often surrounded by an inflammatory vivid red zone, which later may become infiltrated and may become covered with crusts.

The ulcer when completely developed may remain open, or may become covered with a thick crust which extends beyond the margin of the loss of substance The crust may be brownish, reddish or yellowish, or whitish. If the crust is removed, an ulcer is seen with the characters already described.

The ulcer is seldom particularly painful especially if the patient remains at rest It may be tender on pressure pruritus is usually absent except, at times during the healing of the ulcer. The inguinal glands are not enlarged, and lymphangitis is never noted The region of election, as already stated, is the leg, the two lower thirds, but the ulcer may be found on any other part of the body and is not very rare on the feet, hands and arms

Course —The duration of the ulcer is long, seldom less than three to six months, occasionally a year and longer as there is little tendency to spontaneous cure. The ulcer healing leaves a scar which is generally hyperpigmented, but at times hypopigmented. Occasionally no real scar forms, but an infiltrated slightly elevated patch develops or a flattened nodule which has a smooth surface, is slightly reddened and is somewhat painful on pressure. The nodule may from time to time get inflamed after some small trauma, and an ulcer may form. After many months the infiltrated plaque or nodule may become transformed into a real scar by a process of fibrosis.

Clinical varieties —The description given above refers to the usual type of the condition, but several other types may be observed among which the "superficial type" the "plaque and nodular type" the eczematous type" the "generalized pyoderma type"

The superficial type —In this type the initial vesicle or bulla is extremely delicate, and after rupturing a very superficial loss of substance is noted which only slightly involves the corium. The process does not deepen, but extends peripherally until a lesion several centimetres in diameter is formed which has the appearance of a large abrasion rather than a true ulcer The lesion is limited by a thin white

margin this white border being due to the presence of a small amount of pus intra-epidermically all round the lesion

The plaque and nodular type.—A large ovaloid or roundish infiltrated patch 2 to 8 cm or more in diameter is seen somewhat raised over the cutaneous plane with a reddish smooth surface on which occasionally minute ulcers form. In a few cases the lesion becomes frankly nodular

The eczematoid type.—One or more rounded or oval patches are present with the surface covered by crusts which may be small or large On removing the crusts a moist reddened surface is seen. The patches which may be several centimetres in diameter are often well defined, almost marginated and may closely resemble patches of eczema nummulare

The general pyoderma type (Pyoderma mycetoides).—All over the body with exception usually of the face and scalp pustular and crusty lesions are seen, some superficial, some deep The first clinical impression is that of an ordinary generalized pyoderma caused by the usual pyococci, but on examining the patient carefully removing the crusts one or two typical ulcers will usually be found on the legs, which run a very chronic course and from which *Micrococcus (Coccobacillus) mycetoides* may be isolated.

Rarer types.—*The multi-ulcerative septicaemic type* A rare form of mycetoides infection described by CASTELLANI, is one characterized by the presence all over the body of numerous large and rather deep, roundish or ovaloid ulcers the size of a half crown and larger There are prolonged periods of intermittent fever denoting a general infection. In one of CASTELLANI's two cases in addition to *Micrococcus (Coccobacillus) mycetoides* an aerobic actinomyces was present in the ulcers. The strain of mycetoides isolated from these two cases differed in some minor characteristics from the typical *M mycetoides* and CASTELLANI called it *paramycetoid* It is probably only a variant of the typical one

PATHOLOGY

The initial lesion in most cases is a vesicle, situated intraepidermally which rapidly becomes a large vesicle or bulla On the third or fourth day occasionally later the large vesicle or bulla ruptures and by a

process of necrobiosis an ulcer is formed which as a rule does not extend deeply The loss of substance in the corium is surrounded by a zone of infiltration consisting chiefly of neutrophilic leukocytes, lymphocytes, plasma cells and fusiform cells. In histological sections of the margins a marked acanthosis is often noted.

COMPLICATIONS AND ASSOCIATED DISEASES

Complications are extremely rare. In many hundreds of cases CASTELLANI has seen since 1940 he has not noted lymphangitis adenitis erysipelas abscesses or septicaemia. In countries where the true ulcus tropicum is common, cases with both ulcus tropicum and ulcus tropicaloides are not rare.

DIAGNOSIS

In typical cases the diagnosis is not difficult and is based on the presence on the lower two-thirds of the leg of one to four rarely more, ulcers, which run a chronic course, are rather superficial, are roundish or ovaloid 1 to 4 cms. and more in diameter are open or covered by a crust, and are often surrounded by a zone of hyperaemia or at times infiltration the margins are not sensibly elevated nor infiltrated nor usually undermined and the regional glands are not enlarged. The bacteriological examination shows the presence of *Micrococcus (Coccobacillus) mycetoides* the detailed description of which has been given above.

In practice the conditions from which tropicaloid ulcer has to be differentiated are true tropical ulcer (ulcus tropicum) "Veldt Sore" (Ulcus veldis) Septic ulcer (Ulcus septicum) and certain forms of pyoderma vulgare.

Tropical ulcer (ulcus tropicum) is a much more serious condition and its course much longer practically never being less than 1—2 years. It begins with an angry-looking very painful papulo-pustule which quickly breaks down and by a severe process of necrosis an ulcer develops which rapidly extends in depth and surface, at times becoming phagedenic the ulcerative process is much deeper than in tropicaloid ulcer the margins after a time may be somewhat indurated microscopic examination of the exudate will often show the presence of spirochaetes and fusiform bacilli

Veldt sore (desert sore sand sore) —Although the term "Veldt Sore" has been used in the past to cover many different conditions the tendency in recent years has been to limit it to indicate sores of diphtheric origin and SCOTT MANSON BAHR and CASTELLANI and most recent authors use it in this sense The condition begins frequently as a follicular lesion and is often very painful and very tender The bacteriological examination will show the presence of the true diphtheric bacillus (toxic) In some cases of old tropicaloid ulcer diphtheroid bacilli may be present in association with other germs and specific germs but not the true diphtheric bacillus.

The terms desert sore, and sand sore when used without qualification are now considered to be synonyms of veldt sore and the same may be said of the term Barcoo Rot Gift Zeer and Brand Zeer The term Barcoo Rot has been used to cover numerous different conditions. At one time it was used in Australia for ulcerative lesions in cases of scurvy Later it was used to indicate any superficial obstinate sore and also certain forms of ringworm. The use of this term should be discontinued The term Gift Zeer used in certain parts of the Union of South Africa (Transvaal) has been applied to different sores and it is advisable to discontinue its use The term Brand Zeer" is used in some parts of South Africa and should be discontinued for the same reason

Septic sore —Is caused by staphylococci and streptococci and often begins as a small follicular or non follicular pustule or as a group of several small pustules, or as a small or fairly large bulla containing pus which soon bursts One, occasionally more, septic ulcers may develop on the leg after an attack of erysipelas of that limb Septic sore clinically has nothing characteristic, it is generally rather superficial, roundish or oval and may closely resemble veldt sore (diphtheric desert sore) and tropicaloid sore (mycetoid desert sore). A variety of septic sore or septic ulcer is the so-called 'Goodman s chronic streptococcic ulcer which runs a very long course, is generally serpiginous and has undermined margins The regional glands may be enlarged. The diagnosis of septic ulcer is based on the presence of streptococci and staphylococci while *Corynebacterium diphtheriae* and *Micrococcus (Coccobacillus) mycetoids* are absent.

Pyoderma vulgar —Of the chief types of pyoderma, impetigo and

ecthyma, the latter often affects the legs, but it generally begins with a flattened deeply-seated pustule, the size of a small to a large pea, the contents of which dry up in a crust embedded in the skin under which the small loss of substance heals within 2 to 4 weeks leaving a small scar

The bacteriological examination shows the presence of the usual Gram-positive streptococci and often also of staphylococci

Impetigo usually affects the face and no true ulcers are found.

With regard to those forms of generalized pyoderma vulgare presenting features of both impetigo and ecthyma, bacteriological examination will show the presence of the usual pyogenic Gram-positive cocci, (streptococci and staphylococci)

It should be kept in mind however that there is a multiple tropicaloid ulcer with crusty lesions which may closely resemble generalized pyoderma vulgare, but a complete bacteriological examination will reveal the presence in some lesions of the *Micrococcus (Coccobacillus) mycetoides*

Macroulcus perstans —This ulcer described by CASTELLANI (Anals do Instituto de Medicina Tropical, 1949) is characterized by its enormous dimensions torpid course lasting for many years, constant presence of bacteria of the Pseudomonas type and often other pigment producing bacteria of the type Flavobacterium, and Serratia marcescens (Bacterium prodigiosum) in addition to many other germs but usually no streptococci and no staphylococci

Leishmanic ulcers —These are rare on the legs except in South America The microscopic examination will reveal the presence of leishmaniae.

Luetic ulcers —These are of much larger dimensions deeper clean-cut Wassermann test positive.

Varicose ulcers —Varicose veins present, often local eczema, usually pyococci found, *M mycetoides* absent.

PROGNOSIS

The ulcer runs a protracted course, three to six months and occasionally twelve *months and even longer In most cases the general health* is not affected and if the leg is kept bandaged the patient is usually able to attend to his work as the local discomfort and pain are slight

in the majority of cases In some cases however about 10 per cent., hospitalization is necessary

THERAPY

Sulphonamides penicillin and the newer antibiotics among which aureomycin, chloromycetin and terramycin may be tried although they do not appear to give any very striking results. Externally the same antibiotics may be applied in the form of emulsions lotions, ointments and powders

With regard to other methods of treatment it is a mistake to use strong disinfectants and caustics The elastoplast treatment gives bad results The treatment which gives on the whole the best result is a very simple one the patient is kept at rest for three to four days and hot fomentations with boric lotion 2 per cent are carried out twice a day then a dermatol ointment (dermatol 4 g vaseline 26 g) is applied to the sore on a piece of gauze daily the gauze being kept in place by light bandaging Immediately before applying the ointment it is useful to dab the sore with hydrogen peroxide. In some cases when the patient cannot be kept at rest, iodoform is useful, especially when combined with benzoin and charcoal The following lotion gives fairly good results and there is no need of bandaging after applying it Tinct of benzoin 3i ethyl ether 3vi To be applied once or twice daily An Italian preparation containing resins known as "fibroplastina Giorgi" is also useful. Vaccines prepared with the causative organism and given by subcutaneous injection seems to be helpful in some cases but not in all.

PROPHYLAXIS

The slightest abrasion or wound, so often brought about in Africa by spines and stiff short branches of shrubs growing on sandy soil, should be immediately painted with tincture of iodine or mercurochrome or a 2 gentian violet paint or CASTELLANI's fuchsin paint. Long trousers should be worn instead of shorts Vaccines do not give any protection.

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CHAPTER 17

NOMA DE MADAGASCAR (ORAL HOMAMIADANA)

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Tananarive

DEFINITION

"Noma of Madagascar" is a *primary* infectious gangrenous osteo-gingivitis of childhood, usually affecting children in Madagascar during their second dentition and resulting in gangrenous destruction of a large area of the face. *Rarely the condition may start in the oral mucous membrane* The disease is not contagious It is three times as common in girls as boys

HISTORY

In 1816 BARON described *European noma*" also known as *gangrenous stomatitis* as secondary oral gangrene in childhood, originating from VINCENT's angina, scarlet fever rubeola, typhoid fever etc. In 1939 BOULLAT described a similar condition in children from Madagascar where it was called *homamiadana* (*i.e.* of a long duration") This native name however is also given to other chronic ulcerations. Notwithstanding many important differences between oral homamiadana and European noma BOULNOIS and RABEDAORO have given the former the name of *noma de Madagascar*" because of its location, its evolution, its prognosis and its preference to childhood.

EPIDEMIOLOGY

The disease is quite common in the mountainous parts of Madagascar Some cases have been seen in Rumania. It is of great social importance

since it is fatal in 75 % of the cases, or causes severe mutilation and scarring Because only a few adults are seen with relics of oral noma madana, it appears likely that even the survivors of this disease do not live long (See footnote page 456).

AETIOLOGY

The noma de Madagascar is a primary disease usually affecting "healthy" children in contrast with the European noma, which complicates Vincent's angina, scarlet fever etc. In our patients streptococci staphylococci, sarcina, corynebacteria, colibacilli, proteus bacilli, veillonella, ristella or anaerobic micro-organisms were sometimes found but in the more advanced cases PLAUT VINCENT's fusi-spirillar symbiosis was always present. For two out of ten cases this symbiosis was accompanied by streptococci. None of the micro-organisms found proved pathogenic in mice or rabbits with the exception of two cases, where the intramuscular injection of a streptococcus-veillonella caused an abscess, which healed spontaneously In conclusion the bacteriology of noma de Madagascar reveals various saprophytes from the normal human throat. This was checked after investigation of the oral flora in healthy children, in whom also PLAUT VINCENT's fusispirillar symbiosis was common. Because the disease starts in the dental sac, it is perhaps possible that the saprophytic germs have turned pathogenic after having infected the dental gingiva *via* an endogenous route. One is faced with *a similar problem in tropical ulcer* where a phagedaenic process is very probably caused by PLAUT VINCENT's fusispirillar symbiosis, which has so often proved to be harmless. Since pyogenic streptococci have been discovered in the initial stage of the disease it may be possible that this infection has inaugurated the malignant process. BOUILLAT and RAMIANDRASOA have attributed the disease to vitamin C deficiency particularly because vitamin-C therapy lowered the mortality from 80 to 25 %. Later investigations (WOLTZ, PAYET BOULNOIS, PHILIBERT) did not reveal vitamin-C deficiency in children with noma de Madagascar Because 15 of the patients suffered from vitamin deficiency it is very probable that malnutrition plays an important role in the aetiology of oral noma madana. Still one should know that scurvy is unknown in Madagascar and where scurvy is common (*e.g.* French Africa) noma is not known.

In addition epidemiological investigation revealed that noma de Madagascar is quite frequent in the mountainous parts, where the natives are well fed, and that the disease is rare in the coastal regions, where food conditions are worse (ROBIC) Other investigations into malnutrition did not reveal any evidence of importance Perhaps a certain predisposition is present but no particular factor could be detected Again a remark should be made concerning children in



373 Noma de Madagascar

Reunion who live under the same conditions as those of Madagascar without suffering from noma. Noma de Madagascar is not contagious, there is no seasonal rhythm in the epidemiology The disease is more frequently seen among girls than boys (3 1)

SYMPTOMATOLOGY

Noma de Madagascar nearly always affecting children between 1 and

7 years, commences in about 65 % of the cases with a gangrenous acetone-smelling gingivitis which again is initially localised underneath or above the *front teeth*. *Within one week* these teeth are loosened and also pieces of the jaw may be sequestrated. Both jaws may as frequently be affected and in about half of the cases both are simultaneously affected or the one after the other Within two or three weeks *necrosis may* have covered a large area of the oral and facial



374 The same child after vitamin-C therapy which has reduced mortality to 25 %

region. In about 25 % of the cases the disease begins with gangrenous ulceration, rapidly turning to green or black necrosis, the surrounding and underlying skin of which may be still firm. This form often shows a spontaneous arrest after one week, but will continue some days after and cause death within another few days. In about 10 % the disease seems to start from the corners of the mouth (uni or bi lateral) extending *only* over the *skin* and respecting the osseous parts. Noma de Madagascar is a primary disease, only affecting children of normal

body weight who have previously not suffered from a general illness, as is the fact in European noma.

As is common in Madagascar many of the patients have latent malaria or helminthiasis but the noma de Madagascar cannot be regarded as a sequel of these disease as European noma, which occurs when the child is still ill from a primary general illness *Strongyl positive* in about 2 $^{o}_{0}$ of the patients (as is also the case among other children) and the blood does not reveal particular abnormalities

The disease does not affect the pharynx, the tonsils and the tongue



375 Within a fortnight a 3 year old child developed this stage of bomamiadana.

There is a slight non-suppurating adenitis which however may extend along the jaws and be complicated by meningitis, pulmonary disease septicaemia or sinus thrombosis within three weeks

Caries of the teeth cannot be regarded to be the very beginning of this disease but it is of great interest, that it was found that the needle of the syringe giving local penicillin therapy easily penetrated into the alveolar cavity of the diseased teeth until the needle reached the definitive second tooth formation. By this finding substantiated by

my examination, it is probable, that the disease commences in the dental alveoli. As to those rare cases, where the disease begins at the corners of the mouth, this theory is not applicable, but at these places the skin is more vascular and perhaps this may explain the difference.

When not treated early noma de Madagascar is fatal in about 75 % of the cases and because few adults are seen with scars from previous oral homamadama, it is probable that even the survivors of the disease do not live long



376 The same child after three days of intravenous penicillin-therapy (every 6 hours 50 000 U.) In addition 5 % thyrothricine solution was injected in the borders of the ulcer.

DIAGNOSIS

Noma de Madagascar (perhaps a form of tropical phagedaenic ulcer of the oral region) should be differentiated from European noma.

The former is a primary infectious disease affecting healthy

children, non-contagious and almost only known in Madagascar The latter is a secondary condition, being the complication of severe illness, ubiquitous and slightly contagious NOBÉCOURT having described some hospital epidemics[1]



377 Noma in a child of two years old.

THERAPY

Tyrothricin in a 20 % solution and locally applied (every three hours) proved to be of great value in the initial stage as well as in the acceleration of scarring after penicillin therapy

Penicillin locally injected almost always stops the process, only 3 or 4 injections of 50 000 U every 6 hours being sufficient. In more advanced cases 150 000 U can be given and in addition, intramuscular penicillin.

Streptomycin locally applied in the same way as penicillin in a dosage

[1] Noma de Madagascar, a disease in childhood, is not identical with the pure fuso-spirillar non-fetal stomatitis in the adult, which is called *trench mouth* In some cases the latter may be accompanied by involvement of the auditory canal, the genitals and of the smooth skin.

of 250 milligrams in a 20 % solution every 6 hours during 3 to 4 days, proved to be of about the same value as penicillin.

Vitamin C is a valuable adjuvant of the penicillin treatment. In cases of malnutrition general vitamin therapy is desirable.



378. The same child one month after intraosseous streptomycine therapy (1 gram during 3 days). Streptomycine pro ed to be more beneficial than thyrothricine.

The most important *prophylaxis* is propaganda by which the people are instructed to report immediately with children suffering from the slightest oral disease.

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CUTANEOUS DIPHTHERIA

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DEFINITION

Cutaneous diphtheria is an acute infection of the skin by *Corynebacterium diphtheriae* which presents an extremely variable group of cutaneous lesions and which may cause cardiac and nervous manifestations due to systemic absorption of a specific toxin The skin may be involved either primarily (rare) or secondarily by autoinoculation by contact with an infected person or nasopharyngeal carrier or through fomites. The disease is seen more often in children, although it occurs not infrequently in adults and localized outbreaks have been recorded "Jungle sore" indolent ulcers, surgical diphtheria and sometimes even "tropical ulcer" are synonyms for this condition.

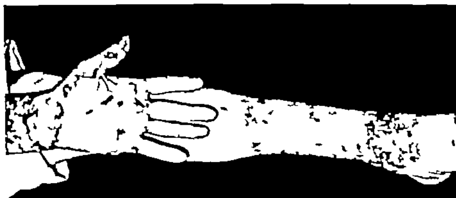
EPIDEMIOLOGY

Inasmuch as diphtheria is endemic at all times and in all climates infection of the denuded cutaneous surfaces is an ever-constant possibility In the temperate zones most cases are seen in the winter months. However in the tropics no such seasonal variation has been observed. It is of extreme interest, in fact, that diphtheria of the respiratory tract is rarely seen in the tropics. One valid explanation of the frequency of cutaneous diphtheria in the tropics is due to the healthy nasopharyngeal carrier and the frequency by insect bites and the slow healing of minor traumatized areas.

PATHOGENESIS

The growth of the *Corynebacterium diphtheriae* produces an exotoxin which can be obtained by filtration methods. This toxin is a protoplasmic poison with specific affinity for nerve tissue and the cardiac muscle. Nephritis and generalized sepsis have also been observed following infection by this organism.

The lesions may involve any part of the body. The extremities, the



379 Cutaneous diphtheria of the legs, hands, and wrists (approximate duration, three months.

(U.S. Army Med. Dept)

genitalia and the intertriginous areas are especially vulnerable. A diphtheritic paronychia has been noted. The lesions are frequently painful, especially when located deep beneath the cutaneous surface.

AETIOLOGY AND BACTERIOLOGY

Corynebacterium diphtheriae is a Gram-positive non-motile, non-sporogenous bacillus, which may occur as extremely pleomorphic slender straight or slightly curved rods. They are rarely uniform, and frequently show club-shaped thickenings at one or both ends.

A positive diagnosis requires the isolation of a virulent organism. The cultural identification should in all cases be followed by animal test to confirm its virulence. The inexperienced should not attempt to make even a tentative diagnosis of diphtheria from direct smears.

Although tellurite is useful in the differential growth in cultural media the application of 2 potassium tellurite to the cutaneous lesion is of such doubtful value that its use is not advised.



380 Cutaneous diphtheria of the left genitocrural area (approximate duration, seven weeks diphtheria antitoxin administered four weeks previously)
(U S Army Med. Dept)



381 Cutaneous diphtheria of the toe web (approximate duration, eight weeks diphtheria antitoxin administered three weeks previously).
(U S Army Med Dept)

SYMPTOMATOLOGY

The typical lesion most often shows a false grayish membrane in a deeply ulcerated area. The edges are swollen. The lesions may also be eczematous, impetiginous, vesicular pustular bullous, or gangrenous. Systemic reaction varies to a great degree. The skin involvement is most often independent of diphtheritic infection of the mucous membranes.

The acute lesions are often associated with positive mucous membrane cultures. The chronic form is frequently superimposed upon "desert sore" in which there are multiple lesions of the elbows, forearms, backs of the hands, knees, legs, and ankles. Post-diphtheritic paralyses and electrocardiographic changes are frequent. The sores are oval shaped, but may be linear. The ulcer is punched out, and has rolled, elevated, hard edges, with a pale blue tinge. The lesion is covered with a leathery membrane which must be removed to make local treatment effective, and to obtain a valid culture.

PATHOLOGY

A fibrino-purulent exudate is formed on the denuded surface, which has been the site of previously traumatized areas. The surface layers



382. Diphtheria of the nailbed.

(Sefer Jerusalem)

then undergo necrosis to fuse with exudate to form the false membrane. This is a grayish structure loosely attached to the surface and composed of fibrin, leukocytes, diphtheria bacilli and other bacteria, dead cells,

and coagulated serum. A raw surface is exposed when the membrane is removed

DIAGNOSIS

Positive cultures of *Corynebacterium diphtheriae* must always be obtained before a final diagnosis can be made. Mixed infections with streptococci, staphylococci and other organisms frequently accompany diphtheritic infection of the skin A diphtheritic lesion most often is noted to have gray sloughing ulcerated areas in the depths of swollen, inflamed wounds However many variations have been observed, such as those previously described

Toxaemia is usually not marked and depends to a great extent on the amount of systemic absorption

THERAPY

Vigorous therapy is indicated in every case of this disease Early recognition of cutaneous diphtheria requires a high index of suspicion. Whenever suspected, valuable time should not be lost while waiting for a culture report 20 000 to 100 000 units of diphtheria antitoxin should be administered intramuscularly the amount depending upon the extent of the lesion and the estimate of the length of time the lesion has existed without specific therapy Local injections of antitoxin into tissues surrounding the skin lesions is not advocated. However local dressings of antitoxin may be helpful.

Concomitant administration of penicillin for a period of 10 to 12 days is beneficial, although it must be realized that neutralization of the exotoxin cannot be accomplished by use of this antibiotic. Penicillin does inhibit most strains of C. diphtheriae *in vitro* and in general should be continued until all signs of infection have subsided.

Methylene blue in powdered form may also be used for topical application, but total reliance on this therapy will result in a false sense of security

Bed rest should be prolonged to at least 6 weeks or until clinical evaluation indicates that activity of the disease has been arrested. Good nursing care is invaluable. A diet high in carbohydrate and proteins, and supplemented with vitamins of the B complex and C are suggested. The neuritis requires appropriate physiotherapy

Prognosis depends on the extent of the lesion and the amount of systemic absorption of the specific toxin. The extent of cardiac involvement can best be ascertained by serial electrocardiographic tracings. Careful neurological examinations at frequent intervals are needed to diagnose the occurrence of neuritis.

PROPHYLAXIS

Rigid quarantine of the infected patient is required as long as any discharge is present. Negative nose and throat cultures should be obtained before quarantine restrictions are to be lifted. Contacts should be known to be Schick negative, or receive a prophylactic dose of 1 000 units of diphtheria antitoxin.

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CHAPTER 19

LEPROSY

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Amsterdam

DEFINITION

Leprosy which exists in two main forms, as will be described below in detail, is an infectious disease caused by Mycobacterium leprae (HANSEN) It is found chiefly in the tropics and, autochthonously hardly ever north of the 40th degree of latitude. The disease spares no race, but occurs especially among poor people living unhygienically According to MANALANG *et al* it starts in youth. Leprosy may be divided into malignant contagious lepromatous leprosy and benign, non-contagious tuberculoid leprosy A number of cases are still indeterminate This will be dealt with later

HISTORY

The origin of leprosy is lost in antiquity One thing is certain until last century (and also during the present century) the disease has often been confused with other dermatoses. The many leprosaria in Europe were in fact, nothing but primitive dermatological clinics"

The biblical word *tsaraat*" means, in fact struck by God" The term was used to cover various affections of the skin and of certain objects The Lord spake to Moses and Aaron, saying, if the priest seeth a white swelling in the skin which hath turned the hair white.

[1] I have to express my indebtedness to Sir LEONARD ROGERS for his helpful collaboration

he shall declare the sufferer to be unclean" (Leviticus 13). And further, "when there is a plague on the head or in the beard of a man or woman, it is scabbiness, leprosy of the head" Leviticus mentions leprosy of clothes and houses (Lev 13 47)

In translating the bible, the word "tsarat" has invariably been rendered by the Greek word "lepra"—which actually means only "scaly"— and which gave to the term an all-comprehensive significa-



383. "Le Roi lepreux" sec. Jeanselme in the Handbuch fur Haut und Geschl. Krankheiten XII 1 See comment under Fig. 4 p. 11

tion. Thus, one of the leprosies was called lepra alphos (*i.e.* psoriasis) another one, lepra asturica (*i.e.* pellagra), yet another (what we now call "leprosy"), lepra arabum, etc.

That Lazarus "whose sores were licked by dogs"[1] (*cf. mal Lazare* and lazaretto) suffered from leprosy finds no support in the text of the New Testament

Attempts have been made—as in the case of syphilis—to discover the country of origin of leprosy Investigations of mummies and

[1] Quite customary therapy for that matter in those days.

pictures from Egypt and Asia remained unsatisfactory, and efforts to discover the origin of the disease from literature were bound to fail, in view of the fact that even today various disease pictures are being confused with leprosy, and that moreover our knowledge of skin diseases is a young science which has grown from a complete chaos of antiquated medicine superstition, pseudo-science, and a host of subdivision systems, under which well known skin diseases were classed, now under one, now under another collective name.

The many wanderings of the nations including the crusades have spread infectious diseases all over the world and it is most difficult, if not indeed, impossible to determine their real cradle. It is generally assumed that syphilis was brought to Europe after the discovery of America, and that leprosy was exported to America by Europeans, together with negro slaves.[1] At about the time of the discovery of America, when syphilis—at any rate the diagnosis M. gallicus—was spreading across Europe, leprosy (at any rate the diagnosis) decreased rapidly. In the 16th century, when London was about the size of the present "City", there were 19 000 "leprosaries" in Europe, but by the year 1700 the disease had suddenly disappeared! (JEANSELME ref. JOHN LOWE.) Treatment of the disease was effected in the most variegated forms. Hideous or frightening lepers (or rather sufferers from skin diseases) were isolated, reduced to beggary; they had to announce their arrival by means of a clapper.

EPIDEMIOLOGY

The present number of leprosy patients is estimated by PERRY BURGESS at 15 000 000 and by ROGERS and MUIR at 5 000 000. About 80 % of known cases are of the benign form. Only about half a million cases, however, are definitely known, out of which about 170 000 are isolated (probably largely unnecessarily). There are ± 10 000 known cases in Europe, ± 2000 of which have been isolated.

The disease is more or less confined to the tropics and the sub-

[1] One oft n hears that American Indians remain free from leprosy. VAN COLL, in 1903, wrote that they are never affected by leprosy. When lepers are found in their camps they are either Whites, or Negroes trying to obtain a cure from the medicine man, or who, after Indian custom, smear their skin with resin.

tropics, and hardly ever occurs north of the 40th degree latitude. Leprosy moreover, is a disease of the poorer, badly fed and unhygienically living part of the population, who—and this is most important—attribute it to such things as magical influence, wrong diet, etc., and who have no fear of infection.

That the disease occurs in regions where the *rainfall* is greatest might perhaps be explained from the fact that, in those areas, people are more inclined to crowd together or alternatively from the life and behaviour of a possible intermediate domestic host. ROGERS suggested on the basis of observations by himself and by MUIR, that



384 The leper belt between 40° north and 40° south latitude.

the innumerable dermal lesions and puncture wounds of the skin produced by mosquito and other insect bites may serve as points of entrance of innumerable lepra bacilli, discharged from the noses of lepromatous patients living with healthy people. The direct inoculation of lepra bacilli by biting insects or the contamination of insect bite wounds etc. by lepra bacilli in the faeces of flies etc. might also be a source of contagion rather than direct inoculation of bacilli by insects. (In 1950 ROGERS suggested at a meeting at Hampstead that the electron microscope might make clear if MOISER's cockroach acid fast bacilli are identical or not with lepra bacilli. The fact that MOISER's

organisms are easily cultivated is perhaps against their being lepra bacilli.)

The regions in which leprosy is most common are Africa, Guiana and Guinea, where over 5 % of the population is affected. Nigeria, the Belgian Congo and the neighbouring Uganda have the highest numbers and rates per thousand. It is interesting to note that, in each



385 From this primary lesion(?) the first analgetic area spread. Note discolouration of the surrounding healthy skin by bergamot oil test.

country a certain region, in each region a certain district, in each district a certain street, and in each street a particular part forms a more intensive focus within another focus: the *endemo-epidemic*; for in countries where the disease is endemic, epidemic foci may appear. Thus, in Paramaribo the surroundings of Charlesburg and Tourtonne, in Jakarta the Tanah Abang neighbourhood are "leprosy districts".

(LAMPE) In Jakarta, LAMPE found that 52 % of cases were to be traced to contagion by housemates The chance of checking leprosy will increase considerably once the malignant cases are isolated under expert guidance and regulation. Every non-isolated malignant patient, however constitutes a source of infection.

The *epidemic occurrence* of leprosy starting from a single patient was observed in the "Louisiana epidemic (1875) (8 cases) the Memel epidemic (1850—1880) (77 cases) the Rodrigues Island epidemic (1870—1920) (23 cases) the Natal epidemic (1843—1895) (± 240 cases) and the Nauru epidemic (1910—1927) (368 cases)

Just as there was a typhoid Mary" there has been a *leprous Betsy*" who, in the Cape Breton" epidemic (1881) had infected 11 persons when her own leprous condition—not until she was 52—came to light. Among these 11 victims were five children of her own and three grandchildren.

The worst epidemic was that in the Pacific island Nauru (1912—1927), where the infection of 30 / of the population of the island originated from a leprosy patient who—contrary to the quarantine doctor s instructions—had been admitted to the island. When, on ROGERS advice, only the malignant cases were isolated, the epidemic was held in check within a couple of years If the Japanese had not put an end to it by artificial means, the epidemic would probably have fizzled out automatically

The *heredity theory of leprosy* (DANIELSSEN and BOECK, 1848) adopted officially by the Royal College of Physicians, London, in 1862, was the reason why some leprosaries were closed down without further ado but the malignant cases thereby liberated caused the disease to spread relatively rapidly (British Guiana).

This heredity doctrine was probably put forward—as in the case of syphilis—because of the fact that a number of children were infected during infancy or youth. RODRIGUEZ failed to find congenital leprosy in any of the 871 children born in Culion (*cit* ROGERS). The degree of a possible hereditary predisposition (L. H SIMONS) is as difficult to determine as for any other disease Most probably—again, as in the case of syphilis—"very early infection has been confused with heredity It is interesting in this connection that PINEDA found

bacilli in the placenta of 50 % of leprous mothers and in the vena umbilicalis of 24 % of their children.

On the African Gold Coast, Negroes believe that the disease is caused by Boassi worms (after the village of that name), for which reason leprosy is also called "*Boassi*" in Surinam (South America), where descendents of African slaves live. Another Surinam name



386 Facies leontina in lepromatous leprosy
(Ozw G. Gesta-Bele Herkpealt)

for it is *kakabe* which, in the African kwa lingo means "unclean".

In Surinam, what is called the "*terefa faith*" is still in vogue. In this faith, the population assumes that the disease is contracted by eating certain ritually prohibited foods, a remnant of a similar Jewish faith, mixed with African fetishism imported by slaves, and according to which these particular foods were held to be the equivalent of some deity. The terefa (trephos, treife = "forbidden eating") is usually discovered in a dream of a mother or an aunt. There are also those who believe that eating certain fruits (in Surinam, the "pomme de

rose" i.e. Eugenia jambos) may give rise to leprosy Thus fruit theory is dominated chiefly by the habit of eating sapotoxins from the roots of the *colocasia plant* (OBERDOERFFER and GEIM)

Much better known than this *fruit theory* is HUTCHINSON's *fish theory* (1863) by which it was assumed that eating decayed fish could cause leprosy[1] DROGNANT LANDRÉ (1869) was the first to assert that leprosy is a contagious disease.

Apart altogether from any theory the fear of the disease has persisted, frequently degenerating into a veritable phobia. Under the urge of this morbid fear the most rigorous isolation measures were passed, with the result that even many non-leprous persons, and, until a short time ago many thousands of patients with non-contagious tuberculoid leprosy were isolated from society It is remarkable, however that this more or less general fear of contagion is offset by its total absence among some peoples they fear the disease, but are not afraid of contagion this is the case for instance, in Surinam (see above) In Asia, too, where some races still believe that leprosy is hereditary there is no general fear of contagion. And it is especially the patients themselves who are quite free from this fear because, with their strongly autistic thinking habits, they refuse to become aware of the danger they present to those around them. It is also interesting to note that the patient s relatives often boggle at the idea of allowing a dangerous source of infection existing in the family to be isolated.

AETIOLOGY

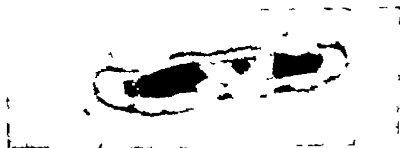
The causal agent in leprosy is *Mycobacterium leprae* discovered by HANSEN in 1871 a straight or slightly bent, acid fast bacillus strongly resembling Bacillus tuberculosis. Like the latter it sometimes occurs singly or spread about the culture, but generally Mycobacteria leprae are found joined together by so-called "*gloea*" like bunches of cigars.

The bacillus can be stained red (in a blue milieu) by the ZIEHL NEELSEN method. Sometimes only the poles of the rod are stained (diphtheroid staining), while in some cases the bacillus is, as it were

[1] A most important finding is that exaggerated dieting on account of the "terefa faith" may cause leprosy to be complicated by a avitaminosis (beriberi and pellagra) (SCHUTTEMAKER).

speckled Sometimes there is a kind of sporiferous formation, re sembling the Much s granules in Bacillus tuberculosis ANGEL IBARS advised the LUTZ staining method by which Much s granule becomes black in a pink coloured bacillus MANSON BAHR distinguishes between dipththeroid, chromogenic acid fast, and non-chromogenic acid fast bacilli A filtrable form and a non-acid fast form have also been described (cited from ROGERS)

In addition to Bacillus tuberculosis Mycobacterium leprae also re sembles the smegma bacillus. In most cases the place where it was found will put the investigator on the right track As a rule, much larger numbers of leprosy bacilli are found in the preparation than



387 Leprosy bacillus seen by the electron microscope Note dense polar bodies at both ends and some scattered in the centre
(Maffatti-Barnes Abrs)

t b bacilli the former usually bundled together into "bunches of cigars Finally M leprae cannot be cultivated—or at any rate, with far greater difficulty than Bacillus tuberculosis According to ANGEL IBARS tubercle bacilli are stained black by YAMAMATO s staining method with silver nitrate, tannic acid and pyrogallolic acid, by which leprosy bacilli are not stained.

In fact notwithstanding the most varying aerobic and anaerobic conditions and widely different culture media the bacillus has never been successfully cultivated. Among the many investigators who believed they had obtained a culture we may mention, BORDONI and UFFREDUZZI (1898) as the first, and CLEGG DUVAL, WEIL and DUCREY (the discoverer of the ulcus molle bacillus) but at the 1938 Cairo Congress it was finally concluded that no satisfactory data had been

obtained regarding the life of the bacillus in vitro (cited from ROGERS) Some more hopeful, albeit indefinite findings, however have been reported from Japan (NAKAMURA 1949) and Brazil, where in June 1951 DE SOUZA ARAUJO claimed to have cultivated and successfully inoculated lepra bacilli (*Roy Soc Trop. Med London*) Studies of the



388. Nodulation of nostrils and earlobes Infiltration of upper lip; low saddle nose.

bacilli with the electron microscope have been published by BISHOP SUTHERLAND and CARPENTER and MARIO MALFATTI (See Fig 387)

Animal experiments—chiefly with rats monkeys and llamas—have never been completely successful. There may be more reason for optimism in experiments in the Syrian hamster (BALFOUR JONES).

Rat leprosy in which the bacilli are never bunched together was

discovered in 1903 by STEFANSKY at Odessa it is common in rats (5 % of Paris rats), but does not occur in man, although MARCHOUX believes he once came across a case. Rat leprosy which is characterized by nodules on the skin and disordered lymphatics and organs, is readily transmitted to healthy rats but, as far as we can ascertain,



389 Facies Antonina with "aspect hebété" in a hybrid of old congenital syphilis and leprosy Note high (syphilitic) and low (leprous) saddle nose nodulation of nostrils and purse string mouth.

is not transmissible to man. For this reason rat leprosy should not be confused with human leprosy DHARMENDRA and MUKHERJEE found that when smears of human leprosy bacilli were exposed to ultraviolet rays for more than six hours the bacilli lost their acid fastness. No such effect was noted in the rat bacillus It is not yet certain whether the ratlepra bacillus can be cultivated.

As regards the *genesis of the infection* this is an open question, the

reply to which we may perhaps approach *per exclusionem* Thus we know from the epidemiology that leprosy is neither a "water-borne" nor an "air-borne" disease that it is found in certain foci which can be ever more exactly localized (LAMPE) Within almost every focus, a new focus can be found a sort of "*focus-in-foco*" infection therefore. A necessary condition for the occurrence of infection (and this is now the generally prevailing opinion) is close contact with a leprosy patient, or *bacillus carrier* (SUTOPO, WATSON), and this contact must be fairly prolonged.

LAMPE found infection by housemates in 52 %, CHATTERJI in 77.5 % of cases examined by them. ROGERS found infection by sexual consortium in 18.28 % and by other home- or bed contact in 39 84 % of his cases LAMPE and BOENJAMIN state that the morbidity rate was 0 7 % after long contact with a tuberculoid case, as against 4 8 % for contact with a lepromatous patient. They found a 29 % morbidity rate for bed contacts, as against 4 % where there was no bed contact (see also the paragraphs containing opinions at the end of this chapter)

DENNEY found, out of 10 000 lepers in Culion, that 35 % were brothers or sisters, 27 % male or female cousins and 11 % children of other lepers. Only 1 % were wives of leprosy patients.

Some authors have described cases of leprosy in persons who had for a long time been wearing clothes previously worn by lepers (HANSEN, KAURIN) others, again, stated that they had observed infection by vaccination (ARNING), by other forms of wound-infection (KAPOSI JEANSELME, EHLERS, HUNDADZE, MARCHOUX and others) or tattooing (BLANCHARD KENSUKE, MITSUDA). In Rogers and Muir s book it is said that vaccination in an early case of leprosy may induce local exacerbations of lesions which are liable to be mistaken for actual infection from vaccination On the other hand, evidence exists of an apparently genuine infection on account of arm to arm vaccination As calf lymph is now almost universally employed, the danger of such rare infections can be averted. We may now safely say that children are most (according to MANALANG exclusively) susceptible to the disease ROGERS found 50 % of his patients to have definitely been lepromatous before their 20th year TALWIK (Esthonia) suspected that 7 % of his youthful patients had been infected by the mother and 5 % by the father The data of SAND and

LIE of Norway are worth quoting as they refer to 2010 children of 587 couples, with 7 % of infections when the father alone suffered from leprosy 14 % when the mother only was infected and 26 % when both parents were infected. (Ref ROGERS and MUIR.)

LARA s work records a morbidity rate of 50 % up to the age of five in children born to leprous parents He affirms that bacteriologi



390 Nodulation of ear lobe called leproma.

cally negative parents may still infect their children, although less frequently than positive ones He holds that the absence of leprosy in children of healthy employees, living with their parents, argues against indirect infection by insects to my mind, however, this fact is far from precluding the possibility of infection by domestic insects such as bed bugs On the other hand, LARA states having seen that the location of the initial lesions in children was on those parts of the body where they most readily come into contact with the parents. Over 50 of the lesions clear up spontaneously without recurrence for 1–13 years, although more than 50 % of all initial

cases were bacteriologically positive In 57 autopsies on children with early lesions he did not find any internal leprosy

Although a leprous primary lesion of the genitals (Gluck) has rarely been observed, it is assumed (Rogers) that leprosy can be transmitted by coition. The possibility should not be excluded that the infection may be caused by kissing or by dripping from the nose



391 Elephantiasis graecorum with shrivelling dropfoot.

Thiroux found bacilli in the vagina of 27 of women patients with lepromatous leprosy The present writer in three cases of women with lepromatous leprosy found no lepra bacilli in the vaginal secretion (two patients were examined three times, one four times). According to Rogers only 2—6 % of persons who cohabited with a leper have contracted leprosy It is, moreover of considerable importance to know the frequency of the sexual contact. Rogers has described three cases which, in the space of two years, contracted leprosy after a single coition with a leprous woman. In a woman who had been living with a leprous man as his wife for over seventeen

years, the present writer found not the slightest symptom of the disease It is interesting to note that, among some peoples (China) there is a superstition that leprosy (like lues) can be "got rid of" and "cured" by "giving it away" to somebody else by coition.

That *close contact* however must imply direct contact is very far from certain for it is possible that the infection is caused by an intermediary host, *i.e.* one which

(a) has a short radius of action (*e.g.* a domestic insect)
(b) causes an indirect infection resembling a direct infection, or
(c) need not be infected itself or if so, may not always have an opportunity to infect a house or bedmate either owing to more or less pronounced or purely accidental circumstances, or because the bacillus at the moment of the intermediary host's bite or sting has not yet reached the maturation point in its cycle.

This, indeed, would explain the *long incubation period* which, therefore consists essentially of a *pseudo-* and a *genuine incubation period.* In other words, the infection is not the result of accumulation of stimuli in the sense that the notion "prolonged contact" means the *prolonged* friction of diseased skin against healthy skin, but in this way that *during* the period of the prolonged contact a "disease-spark" as it were springs across (possibly from an intermediary host) when the bacillus penetrates into the healthy skin. In this connection one should also bear in mind that it may be a long time before a possible intermediary host may happen to be sucking at a leproma, or manages to "collect" bacilli in some other way after which, following the completion of these bacilli's cycle, the host has to find a fresh prey within its own radius of action.

What intermediary hosts are eligible? An insect playing an important role in the lives of unhygienically living people (leprosy is the paupers' disease)? We already mentioned rat leprosy (direct rat bite fleas) The rat is not suspected of being the intermediary host. BARRIOS and URZUA as well as others found that flies in a leper colony carried acid fast bacilli Rather—and the present writer strongly inclines to this view—should one suspect the cockroach and the bedbug MOISER found acid fast rods in 69 % of cockroaches hailing from leprosaries and examined by him. LAMHORN found acid-fast rods as

late as 66 days after cockroaches had been fed on leprous ulcers, and LEBOEUF in 50 % of examined flies. In New Delhi where very little leprosy occurs, more acid fast bacilli were found in the cockroaches than in those from a leper colony and therefore it was concluded that there is no connection between these acid fast bacilli and leprosy (Row) ROSSEL demonstrated chromogenic cultures which germinated



392. Alopecia in lepromatous leprosy (*Muir Bihar*)

well on Löwenstein's medium. These cultures were grown from mosquitos experimentally fed on leprosy patients. ROGERS has summarized the findings in the literature, down to 1 of the bed-bugs examined Perhaps this low figure explains the "long incubation period" (better the long wait before infection)

Infection by objects has often been suspected I believe this to be quite possible, for instance by mats which harbour bed bugs.

Leprosy is frequently combined with scabies. The measure in which the leprosy bacilli accompany Sarcoptes scabiei is unknown. Investigations to find leprosy bacilli in lice obtained from lepers, and in mosquitoes fed on lepers were as a rule unsuccessful (EHLERS, MARCHOUX, CURIE, etc., cited from ROGERS and MUIR).

The following factors argue in favour of the theory that an intermediary host is necessary to cause the infection

1. the infection sometimes occurs only after prolonged contact
2. it does not occur in good hygienic conditions or among the hygienically living social classes
3. the failure of inoculation experiments
4. the disease does not occur among savage races living naked but as soon as they start wearing clothes they may become infected (MANSON BAHR)



393 Nodulation of the prepuce. Note thick crust in this case of lazarine leprosy

Attempts have been made to determine the *incubation period*. This period may be long in appearance only since the precise moment of infection is the unknown quantity. Similarly it is quite possible, for a nurse to be looking after typhus patients for years before contracting typhus although, here, the incubation period is only a few weeks. MANSON describes the case of a man from Mauritius whose wife had never left England. Seven years after his return to England the woman contracted leprosy. This is far from implying that infection occurred at their first meeting after his absence! ARNING has described

the case of a man who had been condemned to death but was given a free pardon on condition that he let himself be infected with leprosy The man got his first leprous patch *at the spot* where he had been infected, and further lesions not until three years afterwards

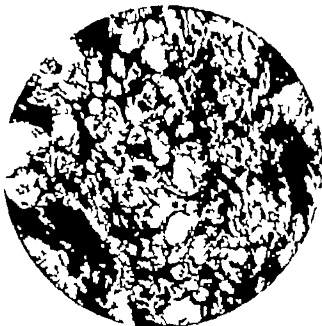
In my own view the *incubation period* should be classified as follows

A Until the moment of appearance of the first symptom.	(1) *the pseudo-incubation period is* from the day when the infected person first had contact with the source. It is possible that this contact was also the cause of infection but it is also possible and, in many cases even probable that infection took place later so (2) *the real incubation period is* from the day on which infection took place until the appearance of the initial lesion. As a rule it is not possible to determine this day certainly not if the two parties have been in contact several times
B Until the moment when the disease is diagnosed as such.	(3) as (1), but to the day on which the disease was diagnosed as such. And this may take years because the patient is unlikely to consult a physician about a small spot" and even if he does the diagnosis will not invariably and immediately be that of leprosy Surely therefore the time during which, according to the patient the lesion has existed must be deducted. None the less this incubation period, like the one sub (1), should be considered "pseudo" (4) from the day of infection until that on which the disease is recognized as such preferably after deducting the length of time that the patient, according to his statement, has had the initial lesion. This incubation period may approximate that defined sub (2).

We should really therefore—as we do in the case of syphilis—speak of *lepra imperfecta* (*i.e.* not recognized as such) *lepra cryptogenica* (*i.e.* with unrecognizable symptoms), *lepra larvata* (*i.e.* symptoms purposely kept secret or concealed) and *lepra incipiens* (*i.e.* the abortive form)

PATHOLOGY

In discussing the pathology of leprosy one is inevitably confronted



394 Lepra or foam or Virchow's cells in lepromatous leprosy

by the two main forms described in some detail in the classification.

Lepromatous or *malignant leprosy* (HANSEN's disease) is characterized by some lymphocytes some mast cells, many epithelioid cells, and, especially by the presence of lepra or foam cells, or *Virchow's cells*. The latter contain many pseudo-vacuoli, which contain a fatty or lipoid substance, similar to the composition of a fatty foreign body granuloma or xanthoma (ARNOLD) and, further large groups of lepra bacilli bundled together into "bunches of cigars". Where these latter

are found we must assume that the lepra cell also exists, or has existed, which entitles us to diagnose lepromatous leprosy If "cigar-bunches" are found in the positive nasal mucus it must be assumed that they originate from a "*leproma*" of the lepromatous leprosy in other words, "positive nasal smear" is, in practically all cases an indication of lepromatous leprosy the nose not being the porte d entrée but, as in tertiary syphilis, the site of predilection of this form of the disease.

There is further atrophy of the entire epidermis, with a flattened



395 Tuberculoid leprosy with giant cell.

papillary layer of the dermis As a rule the atrophic hair follicles and sweat glands are involved in the process.

The *benign* or *tuberculoid* form of leprosy is a "sarcoid" which—conforming to the term tuberculid—may be called "leprid" or "neuroleprid" (UNNA), or "Hansenid" (SIMONS). It is characterized by a tuberculoid tissue structure with giant cells *abundant* lymphocytes, plasma cells and some mast cells. Few or no bacilli are found either in the tissue or in the nasal mucus.

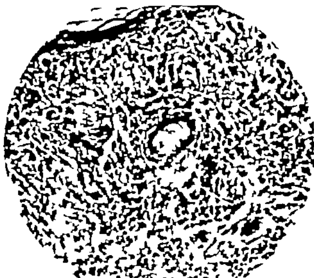
The *indeterminate form* is that which is poor in bacilli and does not (yet) show a specific histological picture. The term *intermediate* (Muir) easily implies a between form, and for that reason is quite as unhappy a name as *lepra mixta* for an alleged mixed form although such forms may exist (See p. 517 and *major tuberculoid leprosy* which shows a tuberculoid histology and leprosy bacilli (not in "cigar bunches") The name *lepra mixta* was formerly used for a type of *lepromatous leprosy being accompanied by neural symptoms*. The term,



396. Giant cells in tuberculoid leprosy

however caused confusion, for which reason it has now been abandoned altogether (see page 571). Nevertheless pictures 399 and 400 in this chapter show a combination of lepromatous and tuberculoid leprosy in the same patient. The old term lepra mixta, however, did not indicate this true mixed form.

In the *acute exacerbation* of (lepromatous) leprosy bacilli may be present in the blood, either in the serum but also in the leukocytes.



397 Langhans giant cell in the upper dermis in tuberculoid leprosy



398 In Bazin's tuberculoid erythema induratum the giant cells are in the lower dermis.

They probably originate from a leproma which has broken through into the blood or lymph circulation. For an epidemiological investigation of leprosy by blood tests however the so-called "thick drop method (SITANALLA) is definitely worthless (*vide* also under visceral leprosy page 521) Some authors deny the existence of bacillaemia (BOENTARAM MORTOADMAJO 1934)



399 Lepromatous evolution of tuberculoid leprosy lepromatous infiltration surrounding tuberculoid lesions. *(Chaussinand-Paris)*

SYMPTOMATOLOGY

Classification

In discussing the symptomatology it is necessary to deal with the different forms separately They are,

(a) lepromatous leprosy
(b) tuberculoid leprosy
(c) major tuberculoid leprosy
(d) the indeterminate form, and
(e) the acute form or lepra reaction.
(f) Lucio s phenomenon.

The notion that the difference between one form and another is merely a matter of degree (DARIER), and that one form may be regarded as a "snapshot" of another is, according to modern opinions incorrect. The concept *lepra mixta* as signifying lepromatous leprosy with neurological symptoms and not a mixed form of the two main groups, has been abandoned as misleading. Nevertheless, a few cases



400. Lepromatous evolution of tuberculoid leprosy: lepromatous infiltration surrounding tuberculoid lesions.

(Chaussinand—Paris)

have been described in which the patient had both lepromatous and, tuberculoid lesions (MEDINA). (See Fig. 399 and 400.) MUIR's book on leprosy contains a picture of such a case (Fig. 4). In the *pseudo-lepra reaction* (*q.v.*) the papules may have both a tuberculoid and a lepromatous histology (DE SOUZA LIMA and DE SOUZA). SCHUJMAN reported a case he has seen undergo transition from tuberculoid to lepromatous

leprosy[1] The name *major tuberculoid lepra* means *bacillary positive tuberculoid leprosy*. ARNOLD states "The flat and elevated "macules" of leprosy apparently represent circumscribed cutaneous areas of acquired allergic hypersensitivity to the nucleoprotein of Myc. leprae

If this hypersensitivity is lacking or inadequate to destroy the organism, the macule is called a lepromatous macule, and it can usually be identified as such by the abundance of bacilli in it and failure to manifest anesthesia or other evidence of nerve damage.

If this hypersensitivity is adequate to destroy the organism, the lesion is then often spoken of simply as a "macule" (or better a tuberculoid plaque) and it can usually be recognized by its relative lack of bacilli and the regular occurrence of evidence of nerve damage throughout its visible extent.

The development of an adequate degree of resistance and allergic hypersensitivity to Myco. leprae results in the establishment of a relatively favourable form of leprosy which has been known as the "anesthetic (DANIELSSEN 1847) maculoanesthetic" (HANSEN 1895), neural" and, more recently "tuberculoid" form.

The failure of development of such a state following infection with Myc. leprae results in the establishment of an unfavourable form of leprosy known as the tubercular (DANIELSSEN) "nodular" (HANSEN) cutaneous and, more recently "lepromatous form.

Such hypersensitivity once developed, usually results in eventual spontaneous cure of the infection it may however be lost, with resultant transition of the case from the tuberculoid to the lepromatous category

The lepromin test appears to be a fairly trustworthy method of measuring this hypersensitivity both in normal skin and in macules."

Lepromatous leprosy

By lepromatous leprosy is understood the contagious malignant form of the disease histologically characterized by the presence of some lymphocytes foam or lepra cells, with cigar bunches" of bacilli. It is in this form too that bacilli are found in the nasal mucus The *lepromin test* is negative

[1] See page 51

In some cases only a single spot is visible for a considerable time in other cases there are multiple lepromas In the latter case there is a marked tendency towards asymmetry which is absent in other forms of the disease, even when the spread is bilateral.

Sometimes the lepromatous lesion starts as an erythematous patch *(rougeur érysipéloïde)* which creeps like a flame *("leprous flame")* having a "teinte triste" which at those places may or may not be



401 Lepromatous leprosy
(Sepher Jerusalem)

analgetic In some cases this erythematous patch resembles a wheal, but it does not itch and is not evanescent. Sometimes there are multiple "wheals" This wheal like lesion is actually a flat leproma, *i.e.* a lepromatous nodule or tuber rich in lymphocytes, lepra cells and bacilli

The leproma is either elastic or hard to the touch. As a rule it is hairless and contains atrophic sweat glands. It is insensible to heat,

cold and pain When held between thumb and index finger and a scratch is made in its skin with a pen, or scraped "incision" (which is called snip" in Hawaii, ARNOLD) serum oozes out which is rich in bacilli (*leper juice*) In some cases one may speak of nodulation, *as* when there is nodular swelling of a nostril, an earlobe, an eyelid, lip nipple prepuce or labium. Needless to say it is essential not to confuse



40. Nodulation of the ears, nostrils, facial skin and lips in lepromatous leprosy Note wrinkling atrophy of fingers, saving the back of the hands and continuing on the arms.
(*Aers–Curaçao*)

tuberous (clinical concept for a firm swelling in both forms of leprosy) with *tuberculoid* (histological concept)

In some cases the leproma is not sharply circumscribed, a large part of the skin being diffusely lepromatous. This may be plainly seen, for instance on the hair-covered part of the head, where in that case, a lepromatous *alopecia* will appear as well as in the face in *facies leonina*.

The ears especially are a favourite location of lepromas, and palpation of the lobes should be carried out in every case of suspected Hansen's disease The lobe, moreover lends itself excellently to the above mentioned serum examination.

Another site of election of lepromatous leprosy—as in the case of tertiary syphilis—is the nose. The nostrils become swollen, and even while nothing abnormal is yet visible outwardly bacilli may be found in the nasal mucus scraped out from the depth of the nose (actually "from a leproma inside the nose"). It is therefore sometimes necessary to scrape with the aid of a rhinoscope (speculum) One sometimes sees a saddle nose or telescope-nose which may (also)



403. Indurations of facial skin note low saddle nose.

be due to complicating syphilis, but which nevertheless may be solely caused by leprosy In leprosy the depression in the nose is usually lower than in syphilis, *i.e.* not in, but below the root of the nose, as a result of necrosis of the septum and the vomer

In the tuberculoid form of leprosy there are no bacilli in the nasal mucus but bacilli are sometimes found in the "major" tuberculoid form, when, however they are not clotted together in "cigar bunches" The idea that the nose is not a site of election but a portal of entry—on account of the fact that bacilli are found there at such an early stage"—must be called in question. *Where cigar-bunches" are found (and this is practically always the case in positive nasal*

mucus) there are lepra cells, and where there are lepra cells there is lepromatous leprosy. Positive nasal mucus, therefore, is a "*type-symptom*" and even an early appearing one, but it is not an early symptom of the entire leprosy group, since tuberculoid leprosy does not yield positive nasal mucus.



404. Multiple confluent nodules in lepromatous leprosy. *(Sagher, Jerusalem)*

In some textbooks one finds epistaxis cited as a *prodrome* of leprosy. It may be possible to construe this prodrome retrospectively, because an ulcer of the conchae or of the septum may set up epistaxis, but since epistaxis is an extremely frequent phenomenon which has nothing whatsoever to do with leprosy, it is as worthless as a prodrome as other, occasionally cited prodromes, such as headache, malaise,

sleeplessness, rheumatic complaints etc. (SIMONS, Dermatologica 1949).

In many cases of lepromatous leprosy there are also lepromas in the eyebrows causing lepromatous alopecia similar to that on the hair covered part of the head. Sometimes it is this *infiltrative alopecia* of the eyebrow which is the first symptom by which leprosy manifests itself. It is also called *madarosis*.

Sooner or later *the eyes* become affected by lepromatous leprosy



405 Tubercles in lepromatous leprosy
(Orr G Costa Belo Horizonte)

when—in contrast to the ocular abnormalities appearing in tuberculoid leprosy—bacilli are found in the eye.

The most frequent *ocular change* is keratitis (either with or without pannus) Sometimes the disease starts with analgesia of the cornea, and in certain cases one may even find a leproma of the cornea. The sclera affected exclusively in lepromatous leprosy (NAAR).

It may be that ptosis can be caused not only by paralysis but also by the weight of a leproma of the conjunctiva. Different authors regard the eye as the portal of entry of the disease (cited from NAAR) It is

interesting to note that NAAR once found many bacilli in a scraping from the cornea, and none in the nasal mucus.

ELLIOT found that lesions of the fundus of the eye preceded cutaneous features in a number of children with lepromatous and tuberculoid leprosy VALE on his part stated that tuberculoid leprosy only causes madarosis atrophy of the orbicular muscle and some conjunctival congestion. In the lepra reaction the cornea, sclera, iris and ciliary body may also be involved (SOTO)

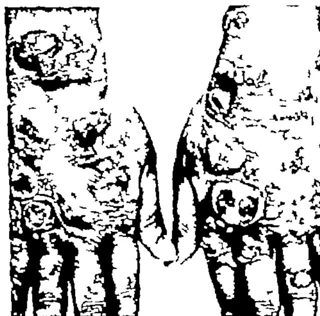


406. Lepromatous nodules of the buttocks (see also Fig 425)
(Murr–Biber)

The *lips* also participate in the lepromatous process in facies leontina. They become swollen, and the resulting fissures are covered with crusts Only in lepromatous leprosy the *mucous membranes* including the tongue are involved. The patient s voice may become muffled *(vox leprosa)* but this does not have the same pathogenesis as the paralytic vox leprosa in tuberculoid leprosy which is due to paralysis of the N lingualis It is obvious that a large number of bacilli can be evacuated by coughing, sneezing or blowing the nose. The lepromatous process may finally assume such dimensions that tracheotomy becomes necessary

Although the face may be most seriously affected, the rest of the body does not go free. The uncovered parts especially suffer most from the disease. It is often assumed that trauma (chronic pressure, *e.g.* of the ear on the pillow) acts as an incitant.

On the chest, abdomen and back the phenomena are less frequent, apart from nodulation of the nipples, which, in the male patient, may



407 Nodules and tubers in lepromatous leprosy
(Sagher-Jerusalem)

set up gynaecomastia. *Genuine gynaecomasty* however, may also appear, as a result of lepromatous destruction of the testes (The testes are not involved in tuberculoid leprosy.) (See Fig. 454 and 455.)

Sometimes infiltrated plaques are seen in the groins, on the abdomen or the back; sometimes, again, the above-described pseudo-wheals and—somewhat more frequently—nodulation of the genitals or part of the genitals (prepuce, scrotum, labia, clitoris) (*vide* also under "coitus")

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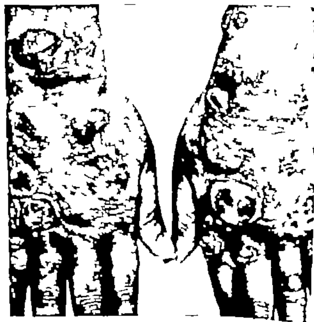


406 Lepromatous nodules of the buttocks (see also Fig. 425) *(Muir-Biher)*

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The affections of the hands and feet are better known. Often the changes are of a purely neurological origin, when they point to tuberculoid leprosy; they may also, however, be due primarily to the lepromatous process, which sometimes leads to elephantiasis. When the bone itself is affected, fingers and toes may become mutilated, but these mutilations are not preceded by "claw hand" which phenomenon is due to tuberculoid leprosy. In those cases where claw hand does



408 Epidermophytosis complicating leprous polyneuritis. Probably the absence of sweat encouraged the growth of the parasite
(Muir-Elber)

precede the lepromatous mutilations, the latter are only due to neurological and trophic disturbances.

The nails become friable and atrophic. In tuberculoid leprosy one sometimes finds "*ongles en bec d'oiseau*".

The *lymph glands* are enlarged and firm and contain a large number of bacilli. Sometimes, however, this adenitis is a consequence of secondary infection and such is wellnigh definitely the case with lymphangitis.

Special mention should be made of *lazarine lepra* (Lucio 1851), the collective term for bullous and ulcerous lepromatous leprosy and the

trophic ulcerations of tuberculoid leprosy Both processes, however are completely different. In the former there is a generalized eruption of lepromas with necrosis. In the latter process there is an ulcerative and necrotizing tuberculoid condition with many bacilli, (*vide* also Lucio's phenomenon, p 514).

In those cases where bullae appear we speak of *pemphigus leprosus* *All organs* particularly the testes may be affected by lepromatous



409 Thickened auricular nerve in a case of tuberculoid leprosy
(Piers Nairobi)

leprosy although in only rare cases has a leproma been found in the brain or in the spinal marrow

The neurological abnormalities, accordingly are usually peripheral. In a few cases bacilli are found in the spinal ganglia. (In rat lepra, bacilli are fairly frequently found in the brain.)

Nerve involvement may occur in both types of leprosy but slowly develops in lepromatous leprosy whereas it develops early and rapidly in tuberculoid leprosy

The patient's *psychic changes* are secondary and caused by the awareness of suffering from this grave disease, by the abhorrence in which he or she is held by others, and by the realization of the possi

bility of becoming and remaining more or less mutilated. In addition, intercurrent diseases or pains and especially the milieu of a leprosary may have a strongly depressing effect. Suicide is relatively rare. It should be said, however, that the patient, being in a somewhat euphoristic state, declines to realize to the full the danger of his disease and tends to underrate it. When the treatment lasts too long for his liking, or gives him too much trouble, he may readily run away



410. Neurofibromatosis (RECKLINGHAUSEN) accompanying lepromatous leprosy (*Muir, Bihar*)

from it, especially when a guaranteed cure is offered him by lay "medical science".

As we stated above, *bacilli in the blood* have been demonstrated in many cases. This is not so in the tuberculoid form, and the presence of bacillaemia has even been denied by those who believe that the bacilli contaminated the preparation because the needle has been pushed through a leproma during the puncture, or become polluted by bacilli present on the skin. This, however, is practically impossible in venous puncture, when the blood flows through the needle. A good method is that according to LOWE and CROWE (cited from ROGERS),

in which citrated blood from a venous puncture is centrifuged and the sediment examined after being de-haemoglobinized by precipitation with 25 % alcohol, and again sedimented by centrifugation. The second sediment is then precipitated with 10 % antiformin, by which the cells are completely destroyed The bacilli may then be found—though not without difficulty—in the third sediment treated with antiformin. LOWE even found, by using this method a few loose bacilli in tuberculoid leprosy The so-called "*thick drop*" test is negative in tuberculoid patients but since it may also be negative in lepromatous leprosy it is, in effect, only a positive preparation that can give us any



411 Arrested lepromatous leprosy Note presence of nail at the left index finger, the white atrophic spots and the wrinkled atrophic skin.

indication, viz that we have to deal with a case of lepromatous leprosy When it is seen—as was observed by LOWE—that there are bacilli on the skin close to the place of the puncture, then this may be taken as probable evidence that the case is one of leprosy rich in bacilli *i.e* either the lepromatous, or the indeterminate form.

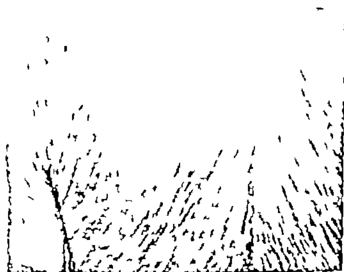
The *erythrocyte sedimentation rate* may be raised

Wassermann's reaction may sometimes be positive in this form of the disease but one should bear in mind that a patient with a positive Wassermann reaction may have in addition to leprosy syphilis or yaws (in the tuberculoid process the Wassermann reaction is not

always found to be positive). *Three quarters of the lepers with a positive Wassermann reaction are due to co-existing syphilis. There remains a small residue of cases in which the positive reaction appears to be due to leprosy alone especially in the nodular forms*" (MANSON BAHR). GOUGEROT calls the blood in lepromatous leprosy a "polyfixateur" because various complement binding reactions may turn out positive.

Often there is *eosinophilia*. When this diminishes the prognosis, according to LEGÉR, is aggravated.

In lepromatous leprosy all excreta and secretions may contain



412. Atrophic wrinkling skin in lepromatous leprosy when severe infiltration with acute inflammatory reaction has subsided. *(Muir Baker)*

bacilli, that is, when the secreting organ is affected by the disease.

Bacilli in the faeces may sometimes be due to an affected throat. Sometimes—especially in the later stages of the disease—there is diarrhoea; this may be due to lepromatous changes in the intestine but in most cases it is due to intercurrent typhus, dysentery or pellagra, the latter being caused by bad nourishment, or disturbed ingestion or no absorption of food.

Bacilli in the urine may occur when the kidneys, urethra or bladder are

affected. They should, however be clearly distinguished from Mycobacterium smegmatis which may also occur in "cigar-bunches" and from Bacillus tuberculosis due to complicating renal tuberculosis.

The sputum may also contain leprosy bacilli When they are not found in cigar-bunches but dispersed they almost definitely suggest the presence of complicating tuberculosis (guinea pig test)

X-ray examination of the lungs is required at regular intervals if only to keep a check on the patient in view of the possible danger of tuberculosis



413 Mutilations in lepromatous leprosy The fingers are shortened owing to osteonecrosis the nails still being visible (thumb and index of the right hand). Note slight atrophy of palmar muscles and blister on right hand.

The liver and the spleen may contain lepromas As a rule this can only be clinically determined in respect of the liver when their size or localization gives rise to disturbances Lepromas in the spleen do not cause clinically demonstrable phenomena

All endocrine glands may be affected by L leprosy and as a result, set up hormonal abnormalities. *Affection of the testes* or *ovaries* may cause sterility It would seem, however that the ovaries are affected at a later stage than the testes. LAMPE found no change

in the fertility of leprous women. The limited number of children of leprous parents should rather in fact, be attributed to the husband's sterility (cited from ROGERS) (*vide* also p. 495 gynaecomastia).

The bone may be primarily affected by malignant leprosy (of this, FAGET and MAYORAL gave an extensive and detailed communication in Radiology' 1944). Nevertheless many if not most, morbid changes in the bones of hands and feet are the result of septic processes which, in their turn, may readily be caused by neurological or trophic



414. Mutilations in lepromatous leprosy. Rudiments of nails still visible. (In tuberculoid leprotic mutilations, due to the analgesia, the nails are absent).

disorders in tuberculoid cases (*vide* also p. 507). LE DANTEC has described "*la percussion douloureuse des os*" as an early symptom.

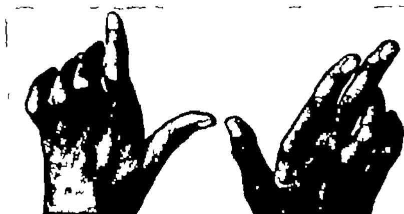
A few words about the sweat glands and the hair follicles. In so far as they are not yet atrophied the former may secrete, in lepromatous leprosy bacilli together with sweat. It would not do, however, to assume this possibility out of hand since the sweat gland very soon atrophies and local anhidrosis is always an early symptom of the disease.

The *general phenomena* may vary considerably and be mixed with

those of tuberculosis, malaria, etc. There are no really specific symptoms As regards pyrexia, *vide acute reaction* p. 511

Anaemia due to lepromatous affection of the bone marrow and the reticulo-endothelial system, has been assumed by amongst others, MUIR. In many cases, however anaemia will be caused (also) by malaria, tuberculosis or other intercurrent diseases, in addition to malnutrition.

Oedema is usually caused by intercurrent beriberi, cardiac dis-



415. Claw hand ("main en griffe") due to involvement of the N. ulnaris and N. medianus and to atrophy of the manual muscles. Note hyper-extension of the metacarpo-phalangeal and flexion of the phalangeal articulations.

ease or some nephrosis (malaria) and in rare cases as a reaction to the therapy (Filaria Bancrofti causes elephantiasis arabum.)

Benign tuberculoid leprosy (leprid-Hansenid)

By the term tuberculoid leprosy (leprid, neuroleprid or Hansenid) we mean the non-contagious benign form of the disease, which, however owing to its neurological disturbances, may nevertheless set up serious disorders The notion "benign" should accordingly be conceived in the sense that the disease, given good hygienic conditions, is often non-progressive, and even shows a marked tendency towards "arrest" or spontaneous cure In addition the term "benign" refers to the fact

that this form of the disease is non-contagious Bacilli are rare in this form and the nasal mucus accordingly contains no bacilli The *lepromin test* is positive. (Even in healthy persons it may sometimes turn out positive.)



416 Crcinat t berculoid leprosy with large rings and tendency to heal

In tubercul id leprosy the lesions are as a rule, localized asymmetrically even when occurring bilaterally The lesion as such, is an erythematous or erythemato-squamous or pigmented, sometimes non-pigmented patch *(v tiligo gravior)* which is insensitive and anhidrotic.

In some cases the depigmented spot is surrounded by a pigmented edge. The erythematous patch, which sometimes creeps over a part of the skin like a flame, has, to an even much greater extent than in lepromatous leprosy the character of a *"rongeur erysipeloïde"*. In this



417 The old lepra maculo-anaesthetica analgetic leukoderma in tuberculoid leprosy

form of the disease, too there is often a wheal-like spot which may even become a node. Not only the uncovered but also the covered skin (buttock) is especially affected.

The tuberculoid form is particularly distinguishable from the lepromatous form (formerly called "tuberous" form), in that it contains

no lepra cells and no bacilli (at any rate definitely no "cigar-bunch bacilli"). Histologically it is characterized by a sarcoid or tuberculoid structure, with many lymphocytes, epithelioid and giant cells. The "macule" is analgetic and thermanaesthetic. The *pilocarpine test* shows it to be also anhidrotic. It is seen, moreover, that the analgetic skin (which sometimes shows no signs at all) on treatment with bergamot oil does not become photosensitive, with the result that it becomes distinctly circumscribed after irradiation, with respect to the surround-



418. Tuberculoid leprosy simulating a lichenified eczema
(Orig. G. Costa-Belo Horizonte)

ing skin which has become "tanned" (SIMONS). There may sometimes be an itching feeling in the analgetic parts.

The mucous membranes are not affected in tuberculoid leprosy.

Alopecia is most rare in this form of leprosy.

JEANSELME has described a dry ichthyotic skin called pachyderma which may appear also in the lepromatous form (MUIR). This phenomenon, however, is probably a symptom of intercurrent avitaminosis.

The most important disturbances are those of the peripheral nerves. They develop early and rapidly and are, for example, the cause of facial paralysis, which *makes the face "hang down limply"*. This

facial paralysis, usually coupled with ptosis of one of the eyelids which, in its turn, may lead to corneal ulcer completes the wretched picture of the *aspect bébété* or *facies Antonine* without the saddle nose and lepromatous nodes such as we know from the facies leontina (*vide* also the eyes in lepromatous leprosy p. 493.)

Paralysis of the vocal cords may cause *vox leprosa* the pathogenesis of which differs from that in lepromatous leprosy (p. 494).

Owing to the grave disturbances in the peripheral nerves (chiefly N. ulnaris and N. medianus) atrophy of the manual muscles sets in, resulting in claw-hand ("*main en griffe*") with hyperextension of the



419 Tuberculoid leprosy
(Orig. G. Costa-Brito Herrgoats)

metacarpo-phalangeal, and flexion in the phalangeal articulations. The nails may sometimes be long and smooth ("*en bec d'oiseau*") in other cases they are hyperkeratotically thickened.

Mutilations too may occur reminding one of the lepromatous form. In these trophic mutilations the nails may still be found on the stumps of the fingers, but—especially after trauma and septic processes—the nails disappear in contrast to what is *sometimes* observed in lepromatous leprosy where the fingers may also be shortened owing to "internal" osteonecrosis while the nails remain more or less intact (*cf.* p. 502). Paralysis of the legs (N. peroneus and N. tibialis post.) causes the notorious "cock's gait" (steppage gait), and trophic disturb-

no lepra cells and no bacilli (at any rate, definitely no "cigar-bunch" bacilli). Histologically, it is characterized by a sarcoid or tuberculoid structure, with many lymphocytes, epithelioid and giant cells. The "macule" is analgetic and thermanaesthetic. The *pilocarpine test* shows it to be also anhidrotic. It is seen, moreover, that the analgetic skin (which sometimes shows no signs at all) on treatment with bergamot oil, does not become photosensitive, with the result that it becomes distinctly circumscribed after irradiation, with respect to the surround-



418 Tuberculoid leprosy simulating a lichenified eczema
(Orr. G. Costa-Bob, Harrewijn)

ing skin which has become "tanned" (SIMONS). There may sometimes be an itching feeling in the analgetic parts.

The mucous membranes are not affected in tuberculoid leprosy.

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JEANSELME has described a dry ichthyotic skin called pachyderma which may appear also in the lepromatous form (MUIR). This phenomenon, however, is probably a symptom of intercurrent avitaminosis.

The most important disturbances are those of the peripheral nerves. They develop early and rapidly and are, for example, the cause of facial paralysis, which makes the face "hang down limply". This

The so-called "*major tuberculoid form*" (ROGERS and MUIR) is a form of tuberculoid leprosy in which nevertheless bacilli (but not in bunches) are found.



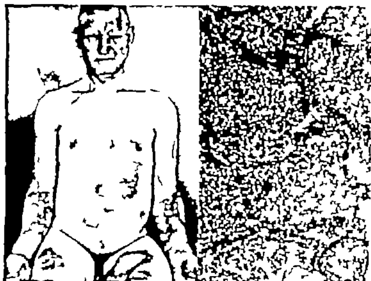
421 Circinate tuberculoid leprosy
(*Kruizinga Groningen*)

The indeterminate form

Apart from lepromatous leprosy in which lepra cells and bunches of bacilli are found and tuberculoid leprosy (either without, or poor in, bacilli) there is another form, which is characterized by the following factors

(a) absence of lepra cells
(b) absence of the tuberculoid structure
(c) the bacilli are few or not to be found and not bundled together
(d) the prognosis is relatively good, because of the tendency to "arrest" or spontaneous recovery

The indeterminate form owes its name to the fact that we do not



422. Major tuberculoid (bacillary positive) leprosy
(*Kruizinga–Groningen*)



423. Leprosy bacilli in tissue of major tuberculoid leprosy 1600 x.
(*Kruizinga–Groningen*)

know under which of the two polar forms to class it. The *indeterminate* form, however is definitely not an intermediate form.

This non-specific, non-determined form is difficult to recognize by the uninitiated. In most cases there is only a rougeur érysipéloïde, an erythema which remains for a long time and is *not* analgetic. Even thermanaesthesia may be absent No bacilli can be found there is no specific histology the lepromin reaction is sometimes positive and sometimes negative and yet—the experienced tropical physician says



424 Acute swelling of the fingers in lepra reaction. Note onycho-atrophy

—"I take it to be leprosy" This form may eventually either cure spontaneously or pass into" either the tuberculoid or the lepromatous form. (See also SCHUJMANN's description of the transformation of tuberculoid into lepromatous leprosy on page 517)

Lepra (lepra-) reaction or acute exacerbation

It may happen that the patient owing to a too aggressive [illegible] (especially with potassium iodide), or by a too strong [illegible] suddenly develops a febrile exacerbation of the disease [illegible] up is called *lepra reaction* It might be compared to a [illegible]
The present writer once saw a young Javanese [illegible]

Pseudo-lepra reaction

De Souza Lima and De Souza, during treatment with sulfones observed erythemato-papular exanthemas without effect on the patient's



426. Declining acute lepra reaction on a predilection place. Same patient as in former figure after one month of rest.



427. Consecutive achromia at one further stage of the previous patient.

general condition. In the papules they sometimes found both tuberculoid and lepromatous processes in the same section. The lepromin

reaction underwent no change. See also pseudo-lepromin reaction in the section on methods of investigation.



428 Tuberculoid leprosy in reaction, showing tubera and an ulcerative plaque. (*Schujman–Rosario*)



429 The same patient after three months of treatment with chaulmogra oil (30 ml weekly) (*Schujman–Rosario*)

Lucio's phenomenon and lazarine leprosy

By *manchada lazarine* or *spotted leprosy* or *lepromatous erythema necroticans* as described by LUCIO and ALVARADO (Mexico 1852) LATAPI understands a diffuse, generalized eruption of lepromatous infiltrations with

necrotlzing lesions, which is most frequently met with in Mexico Histological examination reveals a lepromatous vasculitis and perivasculitis with Virchow's cells and numerous bacilli Alopecia, destruc tive rhinitis and analgesia of the hands and feet are common and the condition is often fatal. MEDINA states that there is an early (within a few hours) intense and short lived response to the lepromin test, contrary



430 Diffuse lepromatous leprosy

(*Fasal–San Francisco*)

to what is expected in other forms of lepromatous leprosy WADE has separated the terms of *lazarine* and *Lucio leprosy* the latter being the diffuse non-nodular spotted type, whilst the name of *lazarine leprosy* should be given to the bullous, centrally necrotising and ulcerative form of tuberculoid leprosy which was described in Cuba by PARDO CASTELLO and PINEYRO. (This form shows numerous bacilli in the necrotic lesions. The lepromine test is positive and the

patient usually recovers) PARDO CASTELLO and PINEYRO however have stated that the term "lazarine" should not be used for a special type of leprosy since bullous and necrotic lesions may occur in both forms. I adhere to this opinion, concluding that Lucio's leprosy is a special form of lepromatous leprosy and that the term of "lazarine"



431–432. Diffuse lepromatous leprosy or Lucio
(*Fasal–San Francisco*)

merely indicates a miserable (after Lazarus) ulcerative form of any type of the disease. Since OBERMAYER, BONAR, ROSENQUIST and GONZALES CHAVEZ found their cases of Lucio's leprosy revealing strong positive serological tests for syphilis, one may perhaps think of a syphilis-leprosy hybrid. (See also page 575.)

TRANSFORMATION OF TUBERCULOID LEPROSY INTO THE LEPROMATOUS FORM

S. SCHUJMAN

Rosario (Argentina)

Transformation of ordinary *non-reactional* tuberculoid leprosy into lepromatous has never been reported. As regards tuberculoid cases *with reaction* having transformed into the lepromatous form some cases have been reported including those with ample documentation by VELASCO in the International Journal of Leprosy 1941 (See also page 484.)

In 1939 discussing the evolution of *tuberculoid leprosy in reaction* I established three types

a. *single reaction* occurring in cases which have shown no recurrence during periods as long as 15 years

b. *periodical reactions* repeated episodes but sometimes with intervals of several years

c. *successive recurrences* (*subintrantes*), so called, because the recurrences are so frequent, that sometimes a new reaction may occur before all the evidence of activity of the previous one has disappeared.

It is these *subintrant* cases, which resemble in their manifest features and evolution the kind variously called "borderline" "intermediate" etc., which sometimes give the impression of undergoing transformation to lepromatous because their erythematous patches sometimes assume a brownish and bronze colour and their borders are somewhat diffuse. However on further observation we have seen that these lesions regressed almost entirely or were followed by a new reaction, but *without* change to an indisputable lepromatous condition.

The true transformation of tuberculoid leprosy in reaction into a frankly lepromatous form, however is still possible, proof of which is supplied by the following case, which I have described fully in the International Journal of Leprosy 1950 (18 1).

M k 42 years old, first seen December 1943. He stated that for o er a year he had had depigmented macular spot on the right foot which about six months



433 Tuberculoid reaction with erythematous tubercles and plaques.



434 5 years late lepromatous transformation with typical diffuse bordered infiltration

previously had become red and that at the same time infiltrated patches appeared on the back and in the face. General condition good. A smear of one of the tubercles showed a few bacilli. No biopsy could be made. Clinical diagnosis tuberculoid leprosy in reaction. Chaulmogra treatment (30 cc weekly).

April 1944 lesions were in frank regression. August 1944 severe reactivation, with lesions all over the body. Colour of the papules and tubercles pinkish, others frankly red, others wine red and ham-like, some surrounded by wide erythematous halo. Nasal mucosa no lesions. In both groins marked adenopathy. No fever, no pain. General condition: slightly ill. Smear of an erythematous



435 T berculoid leprosy in reaction.



435 The same patient after four months of cha lmogra therapy (10 mL weekly).

uberclc revealed disseminated bacilli and globi. Early Fernandez test negative Mitsuda test slightly positive on the 21st day. Biopsy tuberculoid histology.

Despite his promise to continue treatment, the patient was lost to sight for h ears. In July 1949 he returned presenting ordinary lepra reaction of the lepromatous type. He said that, having continued treatment for one year when his lesions had almost completely disappeared. In October 1945 he fractured an arm. After that he neglected treatment for more than year and then at he end of 1946, several erythematous spots appeared on the abdomen. In October 1947 and again in the middle of 1948 two reactions with oedema of the legs malaise and fever. A few tubercles began to ppear especially on the remities. M y 1949 new reaction and, in addition, lesions of the erythema nodosum type. This reaction showed no tendency to regress on the contrary he temperature rose to bout 39 C and also the pains and other symptoms

increased. Involving almost the entire face there was a diffuse lepromatous infiltration. Elsewhere disseminated over the whole body flat plaques. Some were confluent particularly on the extremities.

Attention is especially drawn to the presence of, besides the erythema nodosum elements commonly observed in acute lepromatous reaction, other reaction elements of the size of a hen's egg, elevated, quite red and inflamed and with ulcerated and purulent centres elements resembling abscessed tumours, which at their beginning were red nodosities The nasal mucosa presented erosions and ulcerations on both sides of the septum, which produced bacilli in



437 Section from a lesion after lepromatous transformation showing many Virchow cells in the sub-papillary layer

abundance In the nodular lesions abundant bacilli and globi were also found. Fernandez and Mitsuda test negative Biopsy lepromatous histology with globi and bacilli

As has been said, tuberculoid reaction cases differ greatly in their evolution. In some the reaction regresses definitively leaving no traces or only achromic or atrophic lesions. According to COCHRANE and our own observations, such cases are strongly positive to the lepromin test In other cases there are successive reactions, with be-

tween them more or less prolonged periods of relative inactivity. These latter cases, according to certain authors, may evolve to the lepromatous form, a transformation which is highly exceptional in our experience. I believe that the essential factor which influenced the above-mentioned unfavourable transformation was an organism with low resistance to leprosy as shown by the weak response to the original lepromin. I have never seen a strongly positive Mitsuda reaction become negative. On the other hand, patients giving weakly positive reactions may either change to strongly positive or remain with reactivity unchanged for years or show decrease until the reaction is frankly negative, the patient anergic. The prognosis of tuberculoid leprosy in reaction does not depend on the severity of the reaction or on the number of lesions, but rather on the specific organic resistance indicated by the intensity of the Mitsuda reaction and that *only those reactional tuberculoid cases with weakly positive or negative Mitsuda reactions may evolve to the lepromatous form.*

VISCERAL LEPROMATOUS AND TUBERCULOID LEPROSY

J. CAMPOS R. DE C. – Lima (Peru)
M. MOLINA – Lima (Peru)

In this chapter we will refer only to the *visceral lesions* which are found in the polar forms of lepromatous and tuberculoid leprosy. The anatomical characteristics of the lesions in each of these forms are alike, no matter what organs may be the seat of their development. That means that lepromatous or tuberculoid structures are found with similar characteristics on the skin, in lymph nodes and in viscera.

VISCERAL LEPROMATOUS LEPROSY

In lepromatous leprosy Hansen bacilli are phagocytosed by the macrophages and, once incorporated into these cells, they multiply actively modifying the cellular morphology. At the same time the bacillus

granuloma is observed this results in testicular atrophy and sometimes gynaecomasty KOBAYASHI suggested that loss of testicular function is of diagnostic value when bacilli cannot be found in the skin, mucous membranes and lymph nodes In the kidneys leprosy seldom produces granulomatous infiltration on the other hand nephritis and amyloid degeneration are often observed, and may cause severe degrees of renal insufficiency[1]

VISCERAL TUBERCULOID LEPROSY

When patients with a high degree of resistance or capable of develop-



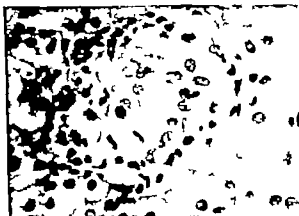
440 Tuberculoid follicle in the liver of a patient with a quiescent form of tuberculoid leprosy

ing such resistance are infected with leprosy reticulo-endothelium cells constitute an unfavourable medium for the reproduction of the bacilli and actually destroy them in this way the morphology of the granuloma is modified and it becomes similar to that observed in tuberculosis that is to say it becomes follicular with epitheloid cells, some multinucleated giant cells and a lymphocytic halo Unlike tuber culosis, however caseation is seldom observed except along the great

R nal ympt ms and albuminuria following a leprous reaction ha e also been described by R u o s

nerve trunks (especially the ulnar) where caseating abscesses are fairly often found.

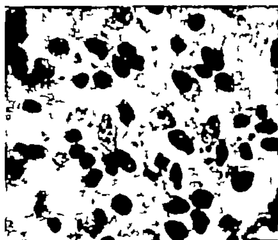
Opportunities seldom occur for the pathologist to examine tissues other than the skin and superficial lymph nodes. This is on account of the favourable prognosis of tuberculoid leprosy and the rarity with which symptoms and signs indicate involvement of the viscera. The result is that many authors claim that tuberculoid leprosy is exclusively a disease of the skin. Thus, BUNGELER states that tuberculoid leprosy is, as has already been said, an exclusive cutaneous disease.



441 Multinucleated giant cell in follicular granuloma of the liver in tuberculoid leprosy

Only in the lepromatous form internal lesions are produced. MULLER affirms that "tuberculoid leprosy of the internal organs does not exist" and MULLER and MERTODIDJOJO believe that when tuberculoid structures are found "in the viscera these are never caused by leprosy". COCHRANE asks "why histological lesions have not been described in the internal organs" and he supposes that the reason is that M. leprae is retained in the subcutaneous tissue without possibilities of dissemination. SOUZA LIMA and SOUZA CAMPOS in their book "Lepra Tuberculoide" only consider injuries of the skin and nerves. They do not mention visceral damage.

In spite of that in the literature there are various reports describing tuberculoid visceral lesions in this form of leprosy such as those of DANIELSEN and BOECK who in 1847 described in their atlas miliary and nodular lesions of serous membranes which they interpreted as of leprous aetiology and the papers of ARNING who found visceral tuberculoid lesions in autopsies of lepers bodies which did not develop tuberculosis when they were inoculated into guinea pigs the opinion which has prevailed is that tuberculoid leprosy is a disease localized to the teguments. This orthodox attitude was clearly ap-



442. Quiescent tuberculoid leprosy. Epithelioid cell focus in mesenteric lymph node

preciated in the inquiry that ARNING himself made in 1936 in The International Journal of Leprosy when he asked leprologists all over the world about their experience with the visceral lesions occurring in tuberculoid leprosy. *Most of the answers denied the existence of these* lesions or they admitted lack of information on this respect. WADE recommended that "special efforts should be made in different regions to resolve the problem definitively"

On anatomical studies made by us (CAMPOS, MOLINA) taking biopsies of the liver of tuberculoid leprosy patients we could discover

the constant presence of tuberculoid miliary foci in variable quantities in every case, more numerous and extensively developed during the reactional stages of the disease than during quiescent periods These findings coincide with those of ARNING and in our opinion, they demonstrate that tuberculoid leprosy like lepromatous leprosy is a general disease not confined only to the skin. The only difference between them is that tuberculoid leprosy produces focal and well localized lesions as a consequence of the resistance of the host. That would explain the lack of visceral clinical signs and symptoms occurring during the evolution of this form of the disease. On the other hand it seems to us that it is unjustifiable to claim that leprosy bacilli cannot outstrip the subcutaneous barrier in the tuberculoid cases when we already know that a hematogenous spread frequently occurs during the course of the leprotic infection.

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MAIN CLASSIFICATION OF LEPROSY

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Amsterdam

(N B The lepromin test is not intended for the diagnosis but as a determinant)

Lepromatous leprosy	*Non-specific or indeterminate form*	*Tuberculoid leprosy*
1 Malignant	1 Not yet differentiated may remain benign, but may also become malignant.	1 Benign.
2. Contagious	2 No bacilli or very few to be found	2. Non-contagious.
3 Lepra cells (Globi)	3 No specific histology	3 No lepra cells, but slight inflammation, or tuberculoid (sarcoid) structure (giant cells).
4 Multibacillar ("cigar bunches") nasal mucus positiv	4 Lepromin test either positive or negative.	4 Few or no bacilli nasal mucus negative.
5 Lepromin test negativ		5 Lepromin test positive.
6 Tendency to symmetry		6. Asymmetry of the (sometimes bilateral) eruption.

7 Little tendency to spontaneous regression.	(MAJOR TUBERCULOID FORM is the multibacillar tuberculoid form (no "cigar bunches")	7 In this form, too, there are sometimes trophoneurotic disturbances which may lead to atrophy contractures and even to mutilations!
		8. Marked tendency to spontaneous regression. In some cases the skin shows nothing specific, when it is possible to delineate the analgetic and anhidrotic zones only by means of the "pin-test" the "cold-warm" or the pilocarpine test. In some cases there are anaesthetic patches without a tuberculoid structure, but only a few symptoms of common inflammation. In other cases the spots are distinctly raised, and one may find a tuberculoid (sarcoid) histological structure. These *leprid* (*neuroleprids Hansenids*) may attain a thickness which gives them the clinical appearance of lepromas.

Tuberous leprosy = clinical concept often lepromatous leprosy
Tuberculoid leprosy = histological concept = leprid = Hansenid.
The tuberculoid form may become tuberous (dermatological concept) without, therefore, being "tuberous" (leprological concept) leprosy
N.B The term "Mixed leprosy" was never intended to imply a combination of the two types but signified that the sites of involvement are mixed, i.e. both cutaneous and nervous (BECKER *and* OBERMAYER) *in lepromatous leprosy* Nevertheless cases of tuberculoid and lepromatous leprosy in the same patient have been described.

METHODS OF INVESTIGATION

Pin prick test In the tropics it is advisable to examine every patch, whether pigmented or depigmented, in respect of analgesia. In less clearly pronounced cases one gets the patient to guess whether he or she is being touched with the blunt or with the sharp end of the pin.

Warm-cold test This serves to determine whether the patient can feel the difference between hot and cold. The sense of temperature is actually disturbed sooner than the sense of pain.

The *pilocarpine test* according to JEANSELME is performed as follows

The patient is given an injection of 20 mg pilocarpine while atropine is held in readiness. After ± 10 minutes the patient starts perspiring to such a degree (this is coupled with greatly increased secretion of saliva) that the loss of fluid may cause him to collapse. For this reason it is advisable to inject atropine, say five minutes after the pilocarpine injection, so that the former's antagonistic action may set in immediately after the pilocarpine begins to act. The time during

which the patient is perspiring is usually sufficient to investigate the anhidrotic patches. JEANSELME advises distinguishing the dry and the wet spots from one another by means of blotting paper but I have not, in most cases found this necessary

The *intradermal mecholyl (chloride) test* serves to demonstrate anhidrosis which has its origin in the most distal parts of the post ganglionic fibres It is performed in the following way

After the affected skin has been painted with 2 % iodine tincture, to which 1 % ricin oil is added ("MINOR's solution") and the skin having become thoroughly dry again, 2—4 drops of the test liquid are in-



443 Lepromatous lesions with many bacilli resembling tuberculoid leprosy (*Muir-Brber*)

jected intracutaneously in such a way that half of the wheal rises on the affected part and half on the healthy part of the skin Starch powder is then immediately sprayed on the iodized patch. After a few seconds only the starch above the healthy part turns blue.

The test-liquid is prepared by dissolving 25 mg mecholyl chloride in 2.5 ml physiological saline solution (ARNOLD Vth Leprosy Congress Havana)

Histamin test (RODRIGUEZ) After applying a drop of a 10 % histamin solution on both the affected and the healthy skin, a slight prick is given into the moistened parts. The healthy skin will then develop a wheal, the diseased part not.

The lepromin test (MITSUDA) This popular test, which may also turn out positive in healthy persons, serves exclusively to differentiate between lepromatous and tuberculoid leprosy (ROGERS). It has a greater prognostic than diagnostic value.

In the malignant form it is negative in the benign form positive. CONTRERAS found a positive reaction in 44 % of non-leprous subjects



444 Analgetic and anhidrotic spots in "invisible leprosy" marked with ink after pin prick and pilocarpine test

(Excerpta Medica II 895). DE FARIA stated that a positive lepromin reaction should be examined histologically only a tuberculoid histology indicating a specific reaction. Local lepromatous reaction of the skin to the lepromin test should be regarded pseudo-positive.

Bergamot oil test (SIMONS). When the patient's skin—which may or may not, show lesions—is smeared over with bergamot oil,

followed by exposure to ordinary sunlight (say for an hour), the bergamot oil will render the skin photosensitive. If part of the skin is affected then that diseased part will not turn black. When this test is combined with the pilocarpine test it is seen that the anhidrotic, analgetic and pigmented zones fall in the same area.

Potassium iodide test The potassium iodide test, which serves to make the vaguer phenomena of the disease more distinctly observable, —*it* acts as a stimulus to the morbid process—is a more or less dangerous experiment. ROGERS and MUIR definitely advise against its use in patients who are in a bad general condition. The test consists of getting



445 Anhidrotic skin of the right shoulder not affected by prickly heat in a patient suffering from tuberculoid leprosy

the patient to ingest 2 g potassium iodide to a glass of water If this yields no result one might try again with 4 g potassium iodide

Wassermann test It is often said that the Wassermann test is found to be positive in lepromatous (also in tuberculoid) leprosy Still this opinion is of no value, since leprosy may not be diagnosed or classified after the blood tests for syphilis To me a positive Wassermann test merely indicates the most probable co-existence of syphilis or yaws.

SHIVELY and KLIDES found that the Kolmer complement fixation test using cardiolipin gave the smallest number of false positive readings compared with

the Kahn standard test, Kolmer complement fixation test and a cardiolipin microflocculation technique. KATZ and co-workers using their Universal Serologic technique found a difference in the precipitation between the sera of lepromatous and tuberculoid leprosy patients.



446. Lateral alopecia (madarosis) in lepromatous leprosy



447. Moth-eaten alopecia in secondary syphilis.

DIAGNOSIS

The tuberculoid form must be distinguished from

(a) the *sarcoid of Boeck* (tuberculoid histology without analgesia. See section on methods of investigation, page 529).



448. This man with tuberculoid leprosy swore justifiably not to have his hair cut before "liberated" from isolation. Note alopecia of eyebrows.

(b) *Vitiligo* (no tuberculoid histology no analgesia)

(c) *Pinta* (no tuberculoid histology positive Wassermann serology no analgesia).



449 Tuberculoid leprosy on the thigh, which at first was regarded as a quininid.



450 Tuberculoid leprosy clinically simulating lupus erythematosus.

(d) *Post-kala azar leishmanoid* (history of kala azar no analgesia.
(e) *"id's"* from toxicoderma, *e g* quininids antipyrinids, etc. (no analgesia, usually no tuberculoid histology)
(See investigative measures in both chapters)
The lepromatous form must be distinguished from
(a) *Leishmaniasis* (Montenegro test positive, Leishman-Donovan bodies, no Virchow cells no bacilli)
(b) *Tertiary syphilis* (positive serology rapid response on anti syphilitic therapy no bacilli no Virchow cells).
(c) *Mycosis fungoides* (no Virchow cells no bacilli)



451 Consecutive achromia in eczema which was initially regarded as macules of tuberculoid leprosy

PROGNOSIS

The prognosis of lepromatous leprosy is considerably more unfavourable than that of the tuberculoid form. When, in addition, the patient is in a bad general condition, or if he suffers from tuberculosis, beriberi, pellagra or any other frequently occurring complication (nephritis pyelitis sepsis), then his prospects of recovery are definitely bad.

This is equally the case in the absence of proper hygienic measures

and adequate therapy For the rest, a lepromatous patient may well go on living for a great many years. Death usually supervenes as a result of either an intercurrent disease or malnutrition, be it that the food is bad, or that the patient suffers from indigestion or no longer normally digests or absorbs his food.

The patient with tuberculoid leprosy has very much better chances.



452. Ichthyosiform phrynoderma, probably due to co-existing vitamin deficiency

Not only does the form of the disease from which he suffers, have a strong tendency to being arrested or to spontaneous cure, but the patient's chances of life are favourable and practically equal to those of a healthy person

PROPHYLAXIS AND PREVENTIVE MEASURES

Although the pathogenesis of leprosy is not completely known,

there are enough factors which, at the present stage of scientific development, should be taken into account.

These factors have led to the following necessary measures

1 *Isolation* of cases of lepromatous leprosy and confinement to certain villages or houses Infectious cases must not be allowed to move about freely in the social milieu and, quite definitely children should be kept well away from them.

Isolation in the home" of malignant cases is a risky undertaking In South Africa, a single home-isolated case infected three members of the family In Rumania, 245 patients, isolated at home,



453 Atrophic skin which should not be confused with the pseudo-ichthyotic or crazy pavement skin from co-existing vitamin deficiency Note normal nails.

caused 83 new infections in the space of six years. The present writer in the case of a leprous woman, personally made all arrangements with the patient s family to enable her to live alone it transpired afterwards that the patient (an intelligent woman) had first gone the rounds of all her friends to say farewell which came to light when a nurse by whom she was befriended suggested that it wasn t quite the thing for her to be kissing everybody

In Surinam the Last Supper service in the churches has been timed to take place in the morning or afternoon, in order to prevent patients at large from attending the service clandestinely and drinking from the common chalice.

2. *Proper hygiene* Special attention must be given to the fight against insect pests such as cockroaches bed bugs (it should be noted that bed-bugs may gain access to books clothes, furniture mats, etc., in the leprosarium)
3. *A follow-up* of patients treated in the out patients department is essential. Examination of other members of the family is also necessary
4. No prophylactic measures to prevent becoming infected with leprosy are known. ROSENBERG SOUZA CAMPOS and AUN have seen healthy children of leprous parents becoming "lepromin positive" 10 to 15 weeks after oral B.C.G. vaccination. For this reason they advise B.C.G. vaccination for the new-born children of leprous parents

QUARANTINE

There is no objection to transporting patients with lepromatous leprosy by boat or plane, providing adequate (not exaggerated) precautions are taken. The cabin occupied by them is subsequently disinfected. Patients with tuberculoid leprosy may travel freely and do not call for any special measures.

Quarantine regulations differ greatly from one country to another. Patients with tuberculoid leprosy ought never to be subjected to such measures.

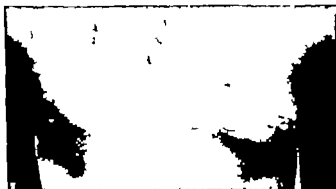
PRONOUNCEMENTS ON THE COMMUNICABILITY OF LEPROSY

1. 75 of all leprosy patients are non-contagious (SLOAN)
2. $^3/_4$—$^4/_5$ of all patients are hardly if at all, infectious, so that isolation of these patients is unnecessary (ROGERS).
3. BARNES has stated that in Southern Nigeria 60 % of the patients had contracted their leprosy from *neural* sources. (This finding proves again that very many neural patients are not tuberculoid cases)
4. A very great deal of infection occurs during childhood and youth (ROGERS, MUIR, MANALANG, COCHRANE and HASELTINE).
5. When children are left with their lepromatous parents for $1^1/_2$ years or more 25 % of them become leprous before they are ten (LÖWE)

6 Leprosy is mainly caused by domestic infection (ROGERS and MOISER)

7 BOENJAMIN found that the transmission of leprosy by family contact with a nerve case is not proved. New cases were found to be due to intercourse with infected persons outside their family. Infection through bed-contact was especially easily effected at the age of 0—14 years.

8 *In the Philippines* BANCROFT *and co-workers found that the danger of infection of persons living in the same house as a lepromatous leprosy*



454 Unilateral gynaecomastia of the hormonal type as is quite often seen (*Uttar-Bihar*)

patient is eight times as great as that of persons of whom it is known that they had no such domestic contact

9 The risk of infection was eight times as high when the patient had contacted a lepromatous case and only twice as high when the primary case was neural (DOULL)

10 *The risk of infection by a tuberculoid case was not found any greater than that among the general population* (BANCROFT).

PRONOUNCEMENTS CONCERNING THE ISOLATION OF LEPROSY PATIENTS

11 It may be advisable and administratively possible to make segregation compulsory (Leprosy Commission, League of Nations)

12 The B.E.L.R.A., for Great Britain, has recommended the segre

gation of all infectious cases that evade proper domestic isolation, and of whom it must be assumed that they still come into contact with children.

13 DAVIDSON considers compulsory isolation to be desirable in Africa where leprosy has a high frequency "The only argument against segregation is its expense." But the rock on which compulsory



455 Pseudogynaecomasty in fact an unilateral leproma. Note papular rash from pseudolepra reaction due to the treatment. (See page 513)

isolation has always split hitherto is the fact that all early and many advanced cases invariably go into hiding (often for life), with the result that the chance of being cured is no longer open to them. For during the period preceding isolation they had ample time to infect others particularly those in their own homes (ROGERS and MUIR)

14 So long as *infectious* cases of leprosy are not segregated a solution will remain impossible (COCHRANE)

15 Leprosy is infectious and can be checked only providing all L patients are segregated (SEN Calcutta)

16 All cases of infectious leprosy at large should be isolated (Cairo Congress)

17 *All regulations dealing with leprosy should be framed so as to allow of early cases being treated without being segregated* (ROGERS and BURGESS).

18 The Army Report dated Oct. 30 1943 for the American army *does not consider leprosy to be to a high degree infectious* According to this report, only close and prolonged contact leads to infection.

19 Non infectious bacteriologically negative cases should be allowed to travel freely (MOISER)

20 The closing down of leprosaries and the abolition of segregation measures as a result of the Report of the Royal College of Physicians (1865) declaring that leprosy was not infectious but hereditary was followed (also because L.-patients were now at large again) by an increase in the incidence of leprosy according to HILLIS, in British Guiana according to MUNRO in St. Kitts according to BROERS—VAN DORT in the Molluccas and the Uliasar islands according to DROGNANT LANDRÉ, in Surinam, and according to EHLERS, in Iceland. In the last named case this was in accordance with the heredity theory of DANIELSSON and BOECK (ROGERS and MUIR)

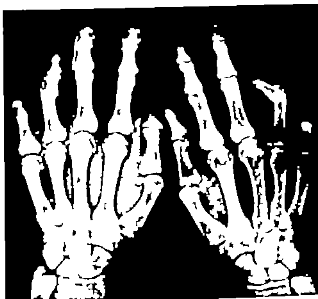
21 Which types of cases should not be discharged?
All L.-cases which were still producing bacilli less than two years previously
All non-infectious patients should go home or in a "sanatorium"
They should however be kept under regular control
Patients *eligible for discharge, but who do not want to leave,* should be prevailed upon with tact and firmness to accept their liberty

22 What we should henceforth do is,
(a) combat outworn, conservative ideas
(b) discharge all tuberculoid patients, classified as follows
(i) those with good prospects, *e g* a good home to go to,
(ii) those without good prospects they will have to be housed in an institution where they will be in the care of either official or private charitable organizations
(c) tuberculoid leprosy should be given another name and
(d) segregation, under humane conditions, of L.-patients.

23 Avoid any form of compulsion that might adversely affect the early discovery and treatment of leprous patients (ROGERS and MUIR)

24 The success of voluntary segregation was shown by the increasing number of requests for admission in Nigeria: in the space of 10 years the number of *applications* rose from 2,500 to 7,000 (Nigeria Conference 1939)

25 The pseudo-fight against leprosy (*i.e.* its compulsory treatment), which results in the flight, or withdrawal, from treatment by a



456 Bone lesions are not pathognomonic of leprosy except in the advanced stages, but are similar to those of other neurotropic nerve diseases, whether of central or peripheral origin (cystformation, osteomyelitis, necrosis, periostitis and enlargement of the nutrient canals). They are rare in lepromatous leprosy when due to primary involvement of the bone marrow or periosteum by Hansen's bacilli or to vascular leprosy of the supplying arteries. In tuberculoid leprosy the lesions are due to the distant involvement of the nerve trunks.
(*Acc. Faget and Mayoral in Radiology 1944*)

number of patients, has, in the present writer's view, three obvious drawbacks, *viz.*

(a) the statistics become confused to such an extent that one might actually begin to believe that compulsory isolation does, indeed, cause an abatement of the disease

(b) a large number of early cases of leprosy withdraw from timely treatment, and

(c) a large number of patients who do not suffer from leprosy at all, but who owing to some lay opinion, have been branded as such, unnecessarily withdraw from medical treatment. A clear case of this type was that demonstrated by SCHUITEMAKER a patient with yaws who might have been cured by a few injections, instead



457 See caption of the previous picture.

of which he remained in hiding for years, from fear of being locked up for being a leper

26 BURGESS makes propaganda for "a world within a world" something like a United States of Leprosaries with their own system of production, exchange, etc. of the commodities produced by them.

27 When a patient in an institution has become negative he or she should be transferred to another department for similar cases If relapsing to positive he should be returned to the original ward, being discharged only after having remained negative for two years (Carville Leprosarium).

28 Tuberculoid patients need not be excluded from the normal social milieu on socio-medical grounds (LAMPE).

29 DAVISON refutes the opinion that neural leprosy is not contagious and holds that neural cases may change to the lepromatous form. In his most important article on the subject, however not sufficient distinction is made between "neural" and "tuberculoid"

30 Segregation should be made voluntary and to some extent attractive (BURGESS)

31 "Once a tuberculoid leper always a benign leper" (BECKER and



458. These bone lesions are due to Besnier Boeck's sarcoidosis. *(Dupont—Brussels)*

OBERMAYER) *The T patient's home is at home*" (SIMONS).

32. The abbreviation V.A.I.L. means 'Village, Agriculture, Isolation, Leprosy' The patients are colonized on plantations and are chiefly engaged in agricultural pursuits. The most obviously suitable product is Hydnocarpus *wightiana* This is accordingly cultivated by lepers in the Congo out of 60,363 cases, 14 983 were isolated mainly in special villages of their own, where they spend their time cultivating medicinal herbs especially the above-mentioned Hydnocarpus tree. (Isolation in the Belgian Congo was effected after registration.)

33. In certain areas in Africa and Korea, men refuse to be put in a

lepers colony without their wives accompanying them. A solution was found for this, in Korea, by suggesting severance of the vas deferens to the man (ROGERS). If full recovery of both husband and wife took place it would be possible to suture the divided vas to renew its function.

PRONOUNCEMENTS CONCERNING DISCHARGE FROM SEGREGATION

34 The following criteria—called, for short, the "Sao Paolo Rules"—have been agreed to according to the South African classification
(a) patients discharged from segregation are checked every four months for two years after discharge
(b) conditional discharge, *i.e.* control every six months for five years after discharge, and
(c) unconditional discharge (CORBONI PECORARO and MERCAU).

35 The term *discharge* according to SHUJMAN should be conceived as having a threefold meaning, *i.e.*,
(a) coupled with the promise to continue the *treatment* ("on parole")
(b) conditional discharge no longer necessary but the patient is expected to report at set times for control and
(c) definite, unconditional discharge.

36 In the present writer's opinion, there should be no such thing as unconditional discharge the patient should always be kept under supervision and control.

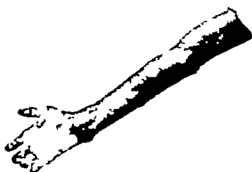
37 In the Philippines, the L patients were discharged as soon as they had been negative for six months but on account of the many relapses the term was increased to twelve months Still later it was further lengthened to two years. Relapses were observed in 9.8 % of cases.

38. Patients who have been bacteriologically negative for two years, without any additional clinical phenomena, the lepromin test being positive and without any "dead bones" on the radiogram, may be discharged (DAVISON, LE ROUX, Pretoria Conference).

39 The possibility of being discharged opens a new perspective in the patient's mind and revives his hope for the future (FIOL)

40 Europeans infected in the tropics should be allowed to return to their home country (Correspondence Intern J of Leprosy).

41 Every tuberculoid patient—who should never have got into a leprosary—should immediately be discharged In this, the lepromin test (provided it is properly performed) is an important criterion Whenever it turns out negative the diagnosis should be one of lepromatous leprosy If positive, one needs only differentiate between the multibacillary form and the (negative) tuberculoid (poor in bacilli) "The line of demarcation as far as segregation is



459 Atrophic musculature of the arm and the hand in arrested tuberculoid leprosy No more than a burnt-out case of polio this man had to be isolated.

concerned should rest on the differential diagnosis between the infective and the non-infective leper (ROGERS and MUIR)

CRITERIA OF CURE

The expression "once a leper always a leper" is outmoded. There are far too many cases to which this text does not apply in the least. Such cases satisfy the following conditions, it being borne in mind, however that the criteria of cure do not correspond to those of "non-infectivity"

1 No bacilli found in either nasal mucus or exploratory excision
2 Lepromin test positive
3 No fresh symptoms for three years in succession, and
4 Potassium iodide test negative.

Some authors prefer the term "arrest" or "quiescent" to "recovery" or "cure"

Repeated examinations over a period of 5 years of all contacts of discovered cases of leprosy should be carried out to ensure that a large proportion of those who have been exposed to infection are detected in the earliest and most curable cases of the disease (Rogers).

CRITERIA OF "NON-INFECTIVE"

The concept "non-infective" is altogether different from that of "recovery" Tuberculoid leprosy is practically non-infective (*vide* the paragraph on aetiology)

Bancroft is of the opinion that a healthy person mixing socially with tuberculoid cases runs no greater risk of contracting leprosy than a person living in a normal milieu. According to him, therefore, these tuberculoid cases ought not to be segregated. It is even highly advisable not to dub them "lepers" but to indicate their trouble by the term of say neuritis (Rogers and Muir) or as "Hansenid"

TUBERCULOID LEPROSY VERSUS BOECK'S CUTANEOUS SARCOID.

For the distinction which should be made between the cutaneous sarcoid of Boeck generalized sarcoidosis of Besnier Boeck Schaumann-Heerfordt syndrome and tuberculoid leprosy one should consult Wade's most interesting article in the Journal of Investigative Dermatology of December 1951 (vol 17 Nr 6). The main difference between tuberculoid leprosy and Boeck's cutaneous sarcoid is the nerve involvement in the former condition, proof of which is the analgesia of the affected skin. Investigations carried out by Wade with Kveim's antigen (obtained from sarcoid spleens), substantiated that the idea of an essential relationship between sarcoid and leprosy is fallacious. The cutaneous reactions to the test were uniformly negative, only an early pseudoreaction having been present in some cases. „The anergy of sarcoid to tuberculin was not seen in leprosy and some sarcoid cases, tested with lepromin did not prove more reactive to it than normal controls, in contrast with the high resistance tuberculoid leprosy" (Wade)

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THE LEPROMIN TEST

DHARMENDRA

Calcutta

ORIGIN AND HISTORY

The lepromin test is the only immunological test of value in leprosy It is also called the *Mitsuda reaction* after its originator It has sometimes been called the *leprolin test* possibly on the analogy of the tuberculin test, but obviously this analogy is not admissible, and the word lepromin is to be preferred (tuberculin from the tuber-cle bacillus, and lepromin from leprom-a)

In 1916 MITSUDA first reported that intracutaneous injections of an emulsion of boiled leprous tissue rich in bacilli usually produced no reaction in nodular leprosy but a marked local reaction in neuro-macular leprosy which took the form of a nodule in the skin, usually appearing two or three weeks after the injection At the International Leprosy Conference, Strasbourg, in 1923 MITSUDA again reported positive results in neuro-macular cases in healthy contacts and in non-contacts, and negative results in nodular cases. He interpreted these results as indicating resistance of healthy persons and neural cases, and the lack of resistance in cases of the nodular type. Between 1924 and 1929 the matter was further investigated by workers like MARIANI B RODHIN, DE LANGEN and DE VOGEL. FUMIO HAYASHI, an assistant of MITSUDA, then took up the work, and as a result of his publication in 1933 in the International Journal of Leprosy the interest in the test became general, and many workers reported on it In some respects early opinions on the lepromin test were confirmed and in other respects they were modified.

About 1940 interest in the lepromin test was revived. The recent work especially of DHARMENDRA and co-workers in Calcutta, and of FERNANDEZ and other workers in South America, has helped to modify and simplify the test, and to explain some of the anomalous features of the original Mitsuda reaction.

PREPARATION OF LEPROMIN

Till recently the methods used by various workers for the preparation of lepromin consisted essentially of grinding the boiled leprosy nodules suspending the ground-up material in 0.5 % carbol-saline,

and eliminating the large particles of tissue by filtration or sedimentation.

In recent years at about the same time two methods have been developed for the preparation of standard solutions of lepromin from separated and dried bacilli and standardised by weight of the dried bacilli One of these methods is that of FERNANDEZ and CASTRO who separate the bacterial powder from a suspension of leprous material in water by taking advantage of the difference in density between lepra bacilli and the tissues. The other method is that of DHARMENDRA by which dried and partly de fatted leprosy bacilli are obtained by extracting the nodules with chloroform. *The chloroform method* of DHARMENDRA gives better results and the details of this method are given below

Pieces of lepromatous material, usually nodules cut from ears, are autoclaved and then ground in chloroform in a glass-mortar The chloroform is pipetted off. The grinding in chloroform is repeated till a smear from the remaining tissue is almost free from bacilli. All the lots of chloroform used in grindings are pooled, and the remaining tissue is discarded. (A smear from the pooled chloroform shows bacilli in very large numbers and the absence of tissue cells or debris). The pooled chloroform extract is stored in a refrigerator for 4 days. At the end of this period the chloroform is completely evaporated on a water-bath, the residual substance consists of lipoids and bacilli The residue is then suspended in ether and the ethereal suspension is centrifugalized in a refrigerator The deposit consists of bacilli. To remove the lipoids more completely the bacillary deposit is again suspended in ether the suspension is centrifuged and the deposited bacilli are separated and dried in vacuum smears made from the dried powder show only bacilli and no tissue. Standard lepromin is prepared by suspending 1 mg of the dry bacterial powder in 10 ml of 0.5 per cent. carbol-saline The suspension is made by putting the powder in a mortar adding few drops of N/10 NaOH, grinding with a pestle and adding the requisite amount of carbol-saline 0 1 ml of the suspension is used for the test.

THE REACTIONS TO LEPROMIN

Lepromin is injected intradermally usually on the outer aspects of the arm. The injection results in

(1) an *early reaction* seen after 1 or 2 days and tending to disappear after 3 or 4 days and

(2) a *late reaction* beginning after about 7 days (sometimes later) and reaching its maximum in 3 or 4 weeks *The late reaction is the classical Mitsuda reaction* The comparative strength of these two

reactions varies markedly with the preparation used for the test with the original lepromin, the early reaction is slight, but the late reaction is marked giving rise to big nodules which often ulcerate with the preparations made from isolated and broken bacilli the early reaction is marked, and the late reaction is slight, the nodule being smaller and often not ulcerating In appearance the early and the late reactions are quite different, and will therefore be described separately

(a) *The Classical Mitsuda Reaction*

The late reaction is the classical Mitsuda reaction. It commences after about one week (sometimes later) and it is characterised by marked local infiltration of the skin, at first somewhat diffuse but becoming more localised as the reaction develops, and producing a definite nodule easily visible and palpable. In cases in which the reaction is marked there is sometimes necrosis in the centre of the nodule, and the skin breaks down with the formation of an ulcer which discharges white cheesy matter, and may take a considerable time to heal. *In many cases however a positive reaction is not associated with ulceration* The nodule attains its maximum size after about three or four weeks, and then gradually subsides, but it may be many weeks before it definitely disappears.

Regarding the criterion of positivity of the Mitsuda reaction a positive reaction may be defined as a progressive infiltration leading to definite nodulation from the second or third week onwards persisting till at least the fifth or sixth week, often longer, the nodule in most cases measuring 5 mm or more in diameter at the end of the fourth week, but occasionally being smaller *Thus the characteristic feature of a positive result is the nature of the reaction nodular progressive and persistent and not its size* The size of the nodule may however be used to grade the degree of positive reaction For example, a nodule of 3 to 4 mm may be called weak positive, of 5 to 7 mm moderately positive, and over 7 mm strongly positive.

(b) *The Early Reaction*

The early reaction is a reaction of the tuberculin type, and is characterised by the appearance of a definite area of erythema about

half an inch or more in diameter around the point of injectio accompanied by an appreciable degree of oedema and thickening the erythematous area The combined effect of the erythema an oedema of the skin is to produce a definite erythematous "flare Till recently the early reaction did not attract much attention, an was not considered to be of great significance. FERNANDEZ was th first worker to make a special study of this reaction and to report th *the early reaction had the same significance as the late reaction* This was late confirmed by other workers.

RESULTS OF THE TEST IN CASES OF LEPROSY

The results of the test in cases of leprosy vary markedly accordin to the type and the sub-type of the disease. Practically all worke are agreed that in typical cases of the tuberculoid type a vast majorit give a positive result, the percentage recorded usually being ove 90 % Similarly in active lepromatous cases, practically all worker have recorded negative results in over 90 % cases there are som workers who believe that a positive result is never seen in cases o the lepromatous type. The results in the types and sub-types of lepros may be summarised as under

Of the active lepromatous cases over 90 % give a negative result while less than 10 % give a weak positive but never a strong positiv result The positive results are common in cases which show clinica and or histological abnormality but are not confined to them.

In cases classified as neuro-anaesthetic or tuberculoid leprosy th incidence and degree of positive results is fairly high some workers however report a low incidence.

In the tuberculoid cases there is a high incidence of positive results, the incidence and degree of positive reactions increasing from simple through tuberculoid not major' to major tuberculoid' with a rising incidence and degree of tuberculoid activity Of the simple cases about 20 give negative results, about 35 % weak positive, and about 45 % moderate or strong positive whereas of the major tuberculoid cases, almost all give positive results, more than 80 % being moderate or strong positive It may be stated that a lesion looking like a tuberculoid lesion in a person with a negative lepro-

min test is almost always a localised lesion of the lepromatous type (smears from this lesion will show a large number of leprosy bacilli)

Of the cases in which the clinical classification is not definite and clear-cut, the result of the lepromin test is variable, and is of help in clearing up the classification. Cases with a negative result are almost always cases of the lepromatous type *provided the test has been adequate* and cases with a positive result are either definitely tuberculoid, or else show a tuberculoid element in histology

Negative Reactions in Lepromatous Cases It is common knowledge that injections of lepromin produce negative results in the vast majority of lepromatous cases This is perhaps the most striking feature of the test. This lack of reaction on the part of lepromatous cases is specific for leprosy bacilli, since their tissues still retain the power to react to injections of other acid-fast bacilli and some irritant substances The cause of this specific lack of reaction is not clear. There are two main lines of thought bearing on this matter firstly that the lack of response of the tissues in these cases is associated with a heavy bacillary infection, and may be similar to the negative tuberculin test seen in very advanced cases of tuberculosis secondly that this lack of activity may be inherent in the tissues and not related to the presence of leprosy bacilli in the body Neither of these hypotheses is entirely satisfactory

RESULTS OF THE TEST IN CONTACTS

Most workers have reported that in the first year of life the results are mostly negative that in the first decade the incidence of positive results is low and that it rises progressively with increasing age. In an investigation in an endemic area in Bengal 295 persons in various age groups were tested, and the following results were recorded

Age Group	Number Tested	Number Positive	Percentage Positive
0–5 years	60	13	21
6–10	80	29	36
11–20	67	48	71
21–30	35	31	89
Above 30	53	52	98
Total	295	173	59

The above results clearly bring out the influence of growing age on the incidence of positive lepromin reactions in contacts

The rising incidence of positive reactions to lepromin with increasing age has been interpreted by most workers as indicating the relative susceptibility of children to leprosy and increasing immunity with increasing age. Some workers believe that this increase in reactivity and resistance to the disease is caused by growing age as such, even apart from exposure to leprous infection. This view is, however not shared by some other workers who believe that the rising incidence of positive reactions with increasing age is caused by increasing chances of exposure to infection.

RESULTS OF THE TEST IN NON-CONTACTS

Positive results with lepromin test have been reported from various countries with no leprosy in persons who have never been in contact with cases of leprosy and in whom the chances of exposure to leprous infection have been practically nil. The incidence and strength of positive reactions in non-contacts is, however lower than in contacts. While some workers, who consider the test as one of specific allergy for leprosy have questioned the occurrence of positive results in non-contacts, other workers who consider the test as one of allergy but not necessarily specific, have attempted to explain the positive results in non-contacts on the hypothesis that infection with other acid fast bacilli, especially the tubercle bacillus, may make persons allergic to the leprosy bacillus.

There are good reasons to postulate the existence of group sensitivity amongst various members of the genus Mycobacterium. In this connection the co-sensitivity of the tubercle and the leprosy bacilli is specially important. The author tested with lepromin and tuberculin 260 persons in various age groups in a part of India where leprosy is very rare and under circumstances that make the chances of exposure to leprous infection very remote It was found that the incidence of positive reactions to both lepromin and tuberculin rose with increasing age *The lepromin sensitivity was higher* (55%) *in the tuberculine positive than in the tuberculin-negative persons* (15%). The facts that 45 % of the tuberculin positive-persons were lepromin-negative

and that 15 % of the tuberculin negative persons were lepromin positive, indicate that infection with the tubercle bacillus is not always accompanied by its sensitivity to lepromin and that sensitivity to lepromin may exist in the absence of tuberculous infection.

NATURE OF THE TEST

The precise nature of the lepromin reaction has been a controversial matter although the consensus of opinion is that a positive reaction is an allergic phenomenon. The various views concerning the nature of the test may be enumerated briefly as follows (1) that the test is a measure of resistance of the tissues to Myco leprae or its products in the antigen used (2) that a positive reaction is an indication of specific allergy and relative immunity produced by previous contact with Myco leprae (3) that the positive reaction may not necessarily indicate specific hypersensitiveness caused by sensitization by various other bacteria of the genus Myco bacterium (4) that a positive reaction although allergic in nature is dependent upon the intrinsic ability of the tissues to react and (5) that a positive reaction is of the nature of tissue response to an irritant.

Space does not permit a discussion of the various views enumerated above, but from the available evidence it may be concluded that a positive lepromin reaction is an allergic phenomenon though the allergy is not always specific, but may be dependent in some persons on sensitization with other acid-fast bacilli, the most important being the tubercle bacillus. The evidence for the test being of an allergic nature may be summarised as under

(i) In appearance the local changes in the skin produced by intradermal injections of isolated antigens are similar to those seen in other allergic reactions, e.g., the tuberculin test. It is believed that the same antigen is responsible for the late nodular reaction seen in the classical Mitsuda test, the lateness and the nodular character of the reaction in this test being caused by the nature of the material injected.

(ii) In healthy persons living in areas heavily infected with leprosy the incidence of positive results is much higher and the degree of reaction is much greater than in healthy persons living in areas where there is little or no leprosy

(iii) The response to the injection of active fractions of Myco leprae is seen not only at the site of injection, but not infrequently in leprous lesions away from the site of the injection, and also at the site of previous injections of lepro-

min. This means that the response is not only local, but not infrequently focal also This is a strong indication of the reaction being allergic.

(iv) The reported sensitization to lepromin of lepromin-negative persons by means of injections with leprosy or tubercle bacillus is strongly indicative of allergy

(v) Definitely tuberculoid and definitely lepromatous cases of leprosy are generally believed to be two immunologically distinct groups. The lepromin test gives almost uniformly positive results in one of these groups (tuberculoid), and almost uniformly negative results in the other group (lepromatous)

(vi) The lack of power to react to the antigen of Myco leprae found in the tissues of patients suffering from the lepromatous type is a specific one. They retain the power to react to other acid-fast bacilli and irritant substances.

THE VALUE OF THE TEST

A few early workers considered the lepromin test of possible value in the diagnosis of leprosy However *it is now generally recognised that the test is of no practical value in the diagnosis of the disease* since positive results are seen in non-cases, and since negative results are seen in cases of leprosy of the lepromatous type. A negative test may sometimes be of limited value in excluding a diagnosis of leprosy in the case of a person having a lesion looking like a typical lesion of the tuberculoid type of leprosy and being bacteriologically negative.

The test is of considerable value in the classification of cases into different types In a vast majority of cases the classification can be made on clinical and bacteriological grounds in such cases the results of the lepromin test confirm this classification. There is a small percentage of cases in which the classification on clinical and bacteriological grounds is not clear cut in such cases the results of the lepromin test are of definite value in clearing up the doubt a definitely positive result would point towards 'lepromatous

The main value of the test however lies in the realm of prognosis The test is of great prognostic value in cases of leprosy of all types, a positive reaction indicating a good prognosis. The prognostic value of the test is however best illustrated in cases of the neural type since in the lepromatous type a great majority of the cases have a negative reaction The test is also of great prognostic value in cases of "doubtful" classification since it clears up the classification and thereby the prognosis

A few workers reported favourably on the use of lepromin in the

treatment of cases of leprosy The consensus of opinion, however, is that it is of no value for this purpose.

Regarding the value of the test in cases of leprosy it can therefore be concluded that the test is of definite prognostic value in all cases of leprosy and is of value in the classification of certain cases. It is of practically no value in diagnosis or treatment.

The test can be of value in another sphere, *i.e.*, to test the genuineness of the alleged cultures of Myco leprae Acid-fast bacilli other than the leprosy bacillus when injected into the skin of patients with leprosy produce positive results in both the tuberculoid and the lepromatous type of cases the leprosy bacillus on the other hand produces positive results in the tuberculoid cases only and negative results in the lepromatous cases. An intracutaneous test with an antigen from a supposed culture of the leprosy bacillus can therefore be used to test the genuineness of the culture.

TREATMENT OF LEPROSY

E. MUIR

Bihar (India)

The treatment of leprosy may conveniently be divided under four sections General, Special, Lepra Reaction, Local.

In undertaking the treatment of a patient with leprosy it is important to assess the extent of the disease, the degree of infection and the amount of resistance to the infection. Especially in dark-skinned patients there may be little or no clinical sign of the disease where bacteriologically there is wide-spread gross infection. In contrast to this resistant cases, especially those with a strong reaction to the lepromin test show very evident circumscribed lesions of the skin, although the bacilli are so few that they are only found with difficulty Obviously the treatment required is very different in these two types of cases.

GENERAL TREATMENT

While the lesser degrees of the milder (neural) type of leprosy are not associated with impairment of general health and will often heal up under special treatment in a comparatively short time, the more severe (lepromatous) type is often accompanied by general debility and anaemia also especially in the more highly endemic countries, malnutrition and complicating infestations are extremely common.

These complications often stand in the way of successful special treatment and their alleviation must be the first consideration. The treatment of accompanying disease a well-balanced diet, appropriate physical and mental exercise and occupation all these form a necessary foundation for special treatment

SPECIAL TREATMENT

The number of drugs that have been used in the treatment of leprosy is a witness to their failure to relieve the disease. Various attempts (MUIR, 1933) have been made to produce immunity by injections of autogenous vaccines such as DEYCKE's nastin. Sera, autohaemotherapy bee-sting, venom, and various forms of protein shock have been tried. The heavy metals, such as antimony mercury gold, copper and arsenic, have their uses especially in desensitizing those who show signs of allergy Other drugs advocated are phenol, sodium salicylate creosote, thymol, ichthyol resorcinol, and iodoform. Considerable discussion has arisen over the value of aniline dyes.

Hydnocarpus oil

Till recently hydnocarpus (formerly known as chaulmogra) oil was the generally accepted remedy for leprosy (MUIR, 1948) This oil is obtained by cold compression from the seeds of Hydnocarpus species, chiefly H wightiana in India and H. anthelmintica in Thailand and Indo China. It was formerly given by mouth, but is now injected parenterally in the form either of the pure oil or of ethyl esters of the fatty acids It is important that the products be fresh and prepared from fresh, ripe seeds otherwise they are painful and badly tolerated. Injections are given intramuscularly subcutaneously and intradermally (the latter into the lesions) or by the combination of these methods. The dose rises from 1 to 10 ml or more, given once or twice a week

according to the tolerance of the patient. Opinions as to the efficacy of hydnocarpus therapy vary considerably in different countries some obtaining good results and others finding it of little or no value. As a rule the treatment is painful and has to be persisted with in cases of the severe type for a number of years. Success has generally been most marked under physicians who are able to inspire their patients to sufficient persistence. The following is the technique for giving intradermal injections (MUIR, 1937).



460. G. H. FAGET under whose regime sulphones were firstly used against leprosy in the U. S. Public Health Service Hospital at Carville (1943).

(Johansson–Carville)

A small syringe is used and, except for reaching the deeper lesions, a short guarded needle is convenient, because it cannot enter the skin too deeply. One half to one minim is injected at each puncture, so that to give the maximal dose of 5 ml, some 80 to 100 punctures are required. Each injection raises a wheal or, if the skin is thick, causes the markings to stand out in increased relief. If a large area has to be covered, the punctures may be spaced more widely. The needle should be sloped to an acute angle with the skin surface and should penetrate not more than 2 or 3 mm except for deeper lesions.

In patients with marked nodules it is sometimes well to begin treatment by infiltrating them, the more diffuse lesions being treated later. With an ordinary hypodermic needle 2 to 5 minims are slowly injected into the middle of the nodule which will first swell and later shrink, with or without liquefaction and discharge. As a rule reinfiltration should not take place till after a month.

Sulphones

The recent introduction of sulphones has marked a considerable

advance in the treatment of leprosy These are the parent substance, 4 4 diaminodiphenylsulphone (DDS), and certain derivatives, of which promin, diasone and sulphetrone have been most used. The first of these to be employed was Promin, given daily intravenously because of its toxicity when administered orally Diasone is equally effective and has the advantage of being tolerated by mouth. Sulphe-



461 Lepromatous leprosy
(Chaussinand-Paris)

trone given by mouth is found wasteful, as only a small fraction is absorbed from the gut, but an equally high blood level can be maintained with about one tenth the oral dose by injecting a watery solution subcutaneously

The parent substance (DDS) was at first supposed to be too toxic for use in leprosy but it was found later to be effective in small subtoxic doses and, when given orally to be absorbed from the gut almost entirely Thus with comparatively minute daily amounts (50 to 250 mg) it is possible to keep up a blood concentration adequate to au se clinical and bacteriological improvement. DDS may also be

injected subcutaneously as a 20 per cent. suspension in pure coconut oil Sulphone derivatives apparently liberate DDS in the body and there is evidence that at least part of their efficacy is due to the action of the liberated DDS

The mode of action of the sulphones is still obscure. The fact that refractory lepromatous ulcers of the skin and upper respiratory tract



462. The same patient after 5 years of chaulmogratherapy

(Chaussinand–Paris)

heal up rapidly suggests that some immediate change takes place in the lepra bacilli. This is also indicated by the early granular appearance of the bacilli which much more slowly in the course of months or years, become thinner and gradually fade out. Smears show the remnants of globi recognisable by their pinkish round mass, either empty or containing a few granular bacilli or a little bacillary debris There is thus presumptive evidence that large numbers of bacilli are rapidly

destroyed by sulphones, though their disappearance from the tissues is delayed. Confirmation of this presumption would be important from the preventive stand-point.

Toxic effects The most important toxic effect is anaemia, to prevent which it is necessary when treating weak, anaemic or badly nourished patients to begin with small doses and increase them according to tolerance, checking the haemoglobin at weekly intervals A percentage



463 Lepromatous leprosy
(Chaussinand-Paris)

of haemoglobin below 60 is considered an indication to reduce the dose or temporarily suspend administration.

The other adverse result of sulphones which makes a diminished dose or temporary suspension necessary is lepra reaction which when slight shows itself in fugitive nodules but when severe may take the form of fever with inflammatory swelling of the cutaneous and sub-

cutaneous lesions, painful swelling of the nerves and aching in the bones Such reactions may be transitory or may last for several days. Reactions are common in the weaker patients, and at the beginning of treatment, but tend to become less severe and less frequent, and, as progress towards recovery advances, cease altogether Sulphone caused reactions though unpleasant for the patient at the time, have the advantage that they speed up the absorption of bacilli.



464 The same patient after 3 months of diasone therapy
(Chaussinand–Paris)

Dosage The average daily oral dose of DDS for a healthy well nourished patient is 4 mg per kilogram of body weight, but in weak patients the initial amounts should not exceed 50 mg More recent trials have shown that 100 mg gradually rising to 400 mg., given twice a week orally in tablet form, is approximately as effective and

much safer than larger weekly amounts. Of the oily 20 per cent. suspension 1 to 1.5 ml is injected twice a week. A 50 per cent. aqueous solution of sulphetrone can be injected subcutaneously twice a week in doses of 3 or 4 ml. The usual daily dose of diasone (given orally) is 0.3 g rising according to tolerance to 2 g

Combined treatment

Reference has been made above to the slow absorption of *Myco leprae* under sulphone treatment, but by combining with it local treatment absorption can be considerably hastened. For this purpose caustics may be applied, such as a 1 in 3 watery solution of trichlor acetic acid, or lesions may be infiltrated intradermally with hydnocarpus oil or esters once or twice a week

LEPRA REACTION

This is shown by inflammatory swelling of existing lesions, the appearance in the skin of new nodules or patches, ulceration or abscess formation of nodules, painful swelling of the nerves pains in the ends of the long bones and other symptoms It is generally accompanied by febrile symptoms. It may be slight or severe and may last from a few days up to several weeks

Lepra reaction is generally connected with general debility and the underlying causes should therefore be carefully searched for and removed. Often some intercurrent disease, such as malaria or dysentery is the cause, or the debility may result from nutritional disorder If fever is a marked feature, the patient must be confined to bed on a light diet Constipation or other bowel disorder must be corrected.

In some cases the administration of alkalies, *e g.*, sodium bicarbonate 60 grains four times daily in water is of value as are also calcium salts given either orally or intravenously Potassium antimonyl tartrate mercurochrome, or fantorin, giving 2 to 4 ml of a one per cent. watery solution intravenously every second day for six days, will generally control the reaction. When the nerves are affected, 5 minims of 1 in 1 000 adrenaline hydrochloride solution injected intramuscularly will remove the pain, as will ephedrine sulphate in 0 5 per cent. sodium bicarbonate solution, or a 1 per cent solution of novocaine infiltrated round the painful nerve Some recommend the injection of 3—5

minims of 75 per cent. alcohol inside the nerve sheath (COCHRANE, 1947)

No one form of treatment is effective in all cases, and one remedy after another may have to be tried before lepra reaction can be controlled. As soon as the condition permits, graduated exercises should be begun. Reactions of this nature seldom occur in patients who are accustomed to take abundant physical exercise (MUIR, 1933)

More recently vitamin B 12 (20 to 30 microgrammes once or twice a week), and also small doses of adrenocorticotropic hormone (ACTH), have been reported as effective in quickly controlling reactions which do not yield to other remedies.

Sulphones in small doses will often arrest lepra reaction when other remedies have failed. On the other hand, as mentioned above, lepra reaction is often induced by sulphone therapy and may take the form either of slight fugitive nodules or of a more severe febrile condition with acute inflammation of lesions. In the former a short suspension of treatment or lessening of the amount will soon clear up the symptoms In the latter confining the patient to bed with low diet, alkalies and laxatives are generally all that is required, though subsidence of reaction may be delayed for some days till the remains of the sulphone have been eliminated from the body As a rule after each sulphone-induced reaction the patient is left in a better state as regards the disease, and as he progresses towards recovery reactions become less in degree and frequency till they cease entirely

LOCAL TREATMENT

Perforating ulcers

The measures to be used in the treatment of perforating ulcers in the sole of the foot depend on the depth of the lesion and on the state of the nerve supply Rest and ordinary dressings will heal a superficial ulcer but if the lesion is deep and involves bone or joint the dead tissue must be removed. Secondary infection and induration of the ulcer often prevent healing If the main nerve supply has been destroyed, healing is difficult. Complete rest in bed and soaking the part in mild antiseptics (water bath or repeated poultices) will cause at least temporary healing if dead bone is absent, but the new tissue is

apt to break down if the patient begins to walk too soon. When a necrotised tarsal bone is at the base of an ulcer a partial or complete tarsectomy will generally bring about healing of the ulcer and may give a permanently useful foot. Patients may give rest to ulcers and yet obtain exercise by using crutches or a wooden bucket leg. Carefully padded shoes are also of use

Hands

Much can be done by splints, proper exercises and occupation to prevent and relieve deformities of the hands. In suitable cases function can be restored by transplantation of tendons (BLAND 1950).

Nerves

Mention has been made above of the use of adrenaline sodium bicarbonate and ephedrine sulphate in the treatment of inflammatory nerves. Diathermy is of use in subacute and chronic nerve conditions. There are also operative methods which may be used with benefit, especially when the condition does not yield to other remedies.

The ulnar nerve as it passes behind the elbow is often bound down to the bone, and the acute swelling in reaction leads to strangulation, severe pain, and sensori motor paralysis. Incision of the constricting tissue relieves the pain and, if the operation is performed in time, gives a considerable restoration of function. Furthermore, in acute reactions the ulnar nerve may be constricted by its own coverings, in which case linear incision of the sheath for three or four inches above the elbow with or without the removal of the thickened fibrous tissue, is very useful. The common peroneal and other nerves may require similar treatment

Abscesses occur in the ulnar and other nerves. They are often multiple and may be central causing swelling of the whole nerve, or may herniate through the sheath. Such abscesses should be incised and the contents scraped out drainage is seldom necessary. Nerve stretching is a useless and harmful procedure

The eye

In leprosy lesions of the eye are due either to leprotic invasion of the eyeball or to interference with the protective function of the

eyelids. The former seldom occurs unless the surrounding skin i
involved. Since there may be considerable change in the eye withou
inconvenience or obvious clinical signs, it is well to test with atropin
all patients with lesions of the face or nose. If there is any sign o
fixation or irregular dilatation of the pupil, atropine should be repeate
occasionally to prevent further fixation. In leprous iridocyclitis eserin
often gives relief by diminishing the congestion

As mentioned above, the introduction of the sulphones has revo
lutionised the treatment of leprosy of the eye. Even with small dos
leprous infiltration which formerly progressed in spite of all treatmen
to complete blindness is now often arrested within a few days o
weeks Care has to be taken, however not to press the treatment to
much to begin with, otherwise a reactive inflammation in the eye ma
be induced by the drug itself. Recently streptomycin, ACTH, an
vitamin B 12 have been found very valuable in intractable inflamm
tory eye conditions in leprosy (MUIR, 1951)

In the second (neural) type there are anaesthesia of the corne
lagophthalmia, ectropion, and consequent inability to protect th
eye-ball. The cornea is apt to become dry and may ulcerate. Liqu
paraffin should be dropped between the lids frequently during the da
and a pledget of cotton-wool soaked in paraffin should be tied ov
the eye at night. In early cases massage of the face round the orbi
and intradermal infiltration with chaulmogra esters round the ey
will sometimes restore the function of the eyelids to a certain exten
Various operations (GASS, 1935) are designed to join the outer pa
of the upper eyelid to that of the lower and thus to protect the ey
ball

The nose

In the majority of advanced cases of lepromatous leprosy the no
is affected, particularly the septum the cartilaginous part is ofte
perforated, and contractions may lead to depression of the nos
Blocking of and discharge from the nose cause considerable distres
Various forms of treatment have been recommended to remedy th
condition. After the mucosa has been anaesthetized with cocain
fulguration may be performed with an insulated unipolar electro
from a diathermy apparatus or the mucosa may be painted with

5 to 10 per cent. solution of trichloracetic acid or chromic acid. Rapid healing and relief usually follow sulphone therapy. In arrested cases it may be possible to improve the appearance of the deformed nose by operation.

DURATION OF TREATMENT

As sulphones have only been in use for a few years it is still too soon to say with any certainty the length of treatment required in the malignant form of leprosy. In the absence of certain knowledge it is well to continue treatment not only till all clinical and bacteriological signs of active disease have disappeared, but also for a considerable time beyond. There is no evidence as yet indicating that *Myco. lepræ* becomes resistant to sulphones, and it is easy for a patient who has tolerated sulphones in moderate doses without toxic signs for a number of years to continue a smaller maintenance dose for a few years more with a view to preventing relapse. In neural cases, with a definitely positive lepromin test, the chance of relapse is much less likely, and once active signs have entirely disappeared further treatment is seldom necessary.

AFTER-CARE

After-treatment and supervision are essential for the prevention of relapses. Patients treated in the favourable circumstances of a residential institution tend to relapse when they return to the less sheltered life, the less regular routine, and—as is often the case—the hardships of their home life. It is well, therefore, that patients should return frequently for inspection during a number of years, and that, if any signs suggesting recurrence appear, they should report at once. To prevent relapse in discharged patients trial is being made of small oral maintenance doses of sulphones, such as 50 to 100 mg a day of DDS. During the period of treatment patients should be educated regarding the nature of leprosy, the danger of relapse, and the importance of maintaining throughout the remainder of life a high standard of general health.

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THE CLASSIFICATION OF LEPROSY

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The tendency of leprosy to assume one or the other of two fundamental forms or varieties is as old as our knowledge of the disease and as new as the most recent publication on the subject. It constitutes the basic fact around which all the multiple efforts at "classification" of the disease have revolved and at which they have all—some less accurately than others—aimed. It is significant, however that attempts at classification began only a century ago with the publication of *Om Spedalskhed* by DANIELSSEN and BOECK in 1847

The reason for this is that, up to that time, the disease now known in English as "leprosy" was known as two different and not certainly related disorders, under the Greek names *elephantiasis* and *leuce* or the Arabic names *baras* and *juzam* respectively *Leuce* had attracted little attention, so that for all practical purposes leprosy existed in only one form *elephantiasis* There was little temptation to try to "classify" this relatively uniform disease pattern, which was that of an intractable progressive, disfiguring tumefactive disorder of the skin and to a lesser extent of the nerves.

DANIELSSEN'S CLASSIFICATION

Then in the middle of the nineteenth century DANIELSSEN and BOECK described *elephantiasis* and *leuce* together under the single name *spedalskhed*, a word which had been up to that time equivalent to

elephantiasis or *elephantiasis Graecorum* (to distinguish it from *elephantiasis Arabum* the filarial lymphedema of the Barbadoes) The word *lepra* or *lepra vulgaris* was used in English texts until as recently as 1875 to designate nummular psoriasis

DANIELSSEN and BOECK had based their classification of leprosy chiefly on morphologic and anatomic features of the disease, dividing it into a "nodular and an anesthetic" variety the former characterized by nodular skin lesions, the latter by nerve lesions. These two forms occurred together more often than separately This classification has dominated most textbooks and the thinking of most physicians for over a hundred years.

HANSEN'S CLASSIFICATION

Toward the close of the century GERHARD ARMAUER HANSEN and CARL LOOFT restored the older biologic division into two forms, which had been so confused by DANIELSSEN and BOECK. They retained DANIELSSEN's term nodular" but substituted for "anesthetic" the term "maculo-anesthetic' to indicate the regular occurrence of skin lesions, as well as anesthesia, in this form of the disease. HANSEN emphasized that (1) both skin and nerve lesions occur in *both* forms of leprosy at some time during their course (2) the two forms of leprosy are mutually incompatible, so that mixed" leprosy does not occur (3) there is no nerve leprosy" as such, nerve lesions occurring in each of the two types.

This was the fundamental pronouncement it has never been superseded or contradicted. Rather it has been supported and strengthened. JADASSOHN s and LEWANDOWSKY's formation of the concept of tuberculoid histological patterns as a characteristic feature of a successful immune reaction against an infection found ready application to the relatively benign maculo-anesthetic lesions. MITSUDA s demonstration of the close correlation between hypersensitivity to injected dead leprosy bacilli and the maculo-anesthetic form of the disease, added an immunological basis for this division to the already extant clinical and bacteriologic criteria In recent years the demonstration that false positive serological tests for syphilis occur in roughly half the cases of lepromatous leprosy and in almost no cases of the benign variety has added further biological evidence of the validity of this division

this is the more significant because BADGER, in Hawaii, showed that such reactions were of equal frequency in cases with predominance of skin lesions and in cases with predominance of nerve lesions.

THE MANILA CLASSIFICATION

In Manila, in 1931 at the small invitational Leonard Wood Memorial Conference, a compromise classification was adopted. It provided two major types of leprosy named cutaneous" (corresponding to "nodular") and "neural" (corresponding to "maculo-anesthetic"), and a "mixed' type which was defined as a variety of the cutaneous" one. The justification for these names was of course the fact that nodular cases involve the skin early and conspicuously and the nerves relatively slowly and inconspicuously whereas the maculo-anesthetic cases involve the nerves relatively early and severely and are frequently characterized by rather inconspicuous skin lesions. The implication contained in such terms, however was grievously misleading their effect was to suggest that the two types of leprosy were "skin leprosy" on the one hand and "nerve leprosy" on the other so that virtually all carefully studied cases (except the very earliest ones) had to be classified—and, in at least one leprosarium under the direction of a delegate to the Conference, *were* classified (usually erroneously)—as mixed" cases.

THE CAIRO CLASSIFICATION

In Cairo in 1938, at the first (actually the fourth) International Leprosy Congress, there was a return to HANSEN s classification. The name cutaneous was happily replaced by lepromatous" and this category of cases was defined, not only morphologically but also in regard to bacterioscopy (abundant bacilli), histology (characteristic granulation tissue), and biological reactivity (negative MITSUDA re action). The term neural" was unfortunately retained, although this category of cases was defined as "all cases of the 'benign form of leprosy with disturbances of polyneuritic nature or macules of nonlepromatous nature (with) evidence of relative resistance to the infection" usually reacting positively to lepromin, usually bacteriologically negative, often histologically tuberculoid. Notwithstanding these explicit statements, and the fact that mixed" leprosy was given

only as a subdivison of the "lepromatous" variety the word "neural" continued to be used by many workers in two quite different senses at one time it would be used to designate this benign variety of the disease, while at another—sometimes qualified as "pure neural"—it would be used to indicate the location of the lesions with the implication, oftener than not, that this *also* indicated the type of leprosy A basic stumbling block at this time was the lack of general agreement that lesions in nerves could be either lepromatous or tuberculoid in their histological characteristics and that they corresponded, in either event to the skin lesions in the same patient.

THE HAVANA CLASSIFICATION

At the Fifth International Leprosy Congress, held in Havana in 1948 the Mexican Brazilian, Argentine, other South American and Cuban dermatologists—who had tried to make themselves heard at Cairo ten years earlier and who had arrived at a general agreement among themselves at Rio de Janeiro in 1947—succeeded in having the word "tuberculoid" substituted for the word "neural" and in getting the concept of mixed leprosy deleted altogether They also succeeded in introducing, and in having generally accepted, the concept of a so-called "indeterminate" (previously designated by them as *incaracteristica*) group of cases, defined as follows

> The indeterminate group Variable with respect to resistance clinical manifestations chiefly in the skin and nerves the skin lesions usually flat macules either hypochromic, erythemato-hypochromic, or erythematous bacteriologically negative as a rule or if positive, with few bacilli lepromin reaction usually negative or moderately positive the lesions histologically of simple inflammatory structure stability much less than in either of the "polar" types and a variable tendency with regard to persistence, regression, progression, or transformation into one of the "polar" types. These cases are usually non-infectious"

This definition covers only "initial" indeterminate cases, according to MUIR's concept he would extend the concept to include "intermediate" or transitional cases (lepromatous becoming tuberculoid, or tuberculoid becoming lepromatous), and "vestigal" indeterminate cases (unclassifiable by reason of advancement of healing). RYRIE feels

the whole concept is inapplicable to many cases seen in Malaya, and suggests dividing the disease into primary (early macular), secondary (tuberculoid) and tertiary (lepromatous) forms—a classification which is in a sense, if "early macular" be taken to mean "indeterminate" the same as the Havana classification. DHARMENDRA prefers retention of a clinical classification: lepromatous, neural anaesthetic, neural macular, neural tuberculoid.

The definitions of the lepromatous and tuberculoid categories approved and adopted at the Havana Conference are as follows:

The lepromatous type. Minimal resistance to the existence, multiplication and dissemination of the bacilli, constant presence of large numbers of bacilli in the lesions, with a distinctive tendency to form globi; characteristic clinical manifestations in the skin, the mucous membranes (especially of the upper respiratory tract and eye) and/or the peripheral nerves, together with involvement of other organs; regular failure to react to lepromin; pathognomonic granulomatous structure of the lesions; marked stability of type and a tendency to progression. These are the "infectious" or "open" cases.

A special variety of lepromatous leprosy, common in Mexico and Costa Rica but rare elsewhere, is so-called "*diffuse lepromatosis*" (LATAPI) or "*lazarine leprosy*" (LUCIO). In many respects, LUCIO's variety of leprosy is like ordinary lepromatous leprosy: with gradual onset, generalized involvement of the skin, relatively symmetric nerve involvement, nasal lesions, loss of eyebrows, abundant bacilli, histologically lepromatous infiltrate, frequently positive serological tests for syphilis, negative FERNANDEZ (forty-eight hour) and MITSUDA (three week) reactions to intradermally injected lepromin and progressively downhill course (in untreated cases). In other respects it is unlike ordinary lepromatous leprosy: lesions of the eye are rare, laryngeal lesions are rare, intradermally injected lepromin elicits a severe reaction at the injection site in four to five hours (the MEDINA reaction), vesicular lesions (the "spots") occur followed by shallow necrosis, and, perhaps most extraordinary of all, the classic and almost definitive lesion of lepromatous leprosy, the leproma itself, never occurs. It is *lepra lepromatosa sine leproma*. (See also page 514.)

The tuberculoid type. High resistance to the existence, multiplication and dissemination of the bacilli; as a rule, bacteriologically

negative or if positive, with few bacilli except in reactional states characteristic clinical manifestations, mainly in the skin and nerves, tending to be limited in extent and varying in degree with the reactivity of the tissue reactivity to lepromin in a very high percentage of cases nearly always a tuberculoid granulomatous structure in active lesions marked stability and a strong tendency to spontaneous regression in the absence of repeated reactions. These cases are usually "non infectious or "closed"[1]

It is important to note that no single criterion can be employed to determine the classification of any given case of leprosy it has been wrongly said that the uncharacteristic or indeterminate cases have in common only the possession of histological rejection slip" The classification should ideally be based—and in many cases *must* be based—on the consideration of all factors (1) clinical appearance, (2) neurological findings especially in relation to skin lesions, (3) bacterioscopy (4) histology (5) biological status (reactivity to the nucleoprotein of the leprosy bacillus, as indicated by the FERNANDEZ and MITSUDA reactions) and finally perhaps (6) clinical course of the disease In some cases, clinical appearance alone may seem pathognomonic of one or the other type of the disease, and usually the other criteria will confirm the clinical impression. In cases presenting simple macular lesions, this is often not the case further evidence must be secured if such further evidence is consistent, and points toward one or the other type of leprosy a classification as to type may be made but if it is inconsistent (*e g*., few bacilli banal histology and positive MITSUDA reaction or no bacilli banal histology but negative MITSUDA reaction) then the case may have to be labelled, for the time being at least as indeterminate"

[1] SIMONS called this form *Hanseníd*.

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CHAPTER 20

CUTANEOUS TUBERCULOSIS AND SARCOIDOSIS IN THE AMERICAN NEGRO AND IN INHABITANTS OF TROPICAL COUNTRIES

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CUTANEOUS TUBERCULOSIS

EPIDEMIOLOGY

Little statistical data on the frequency of cutaneous tuberculosis in tropical countries are available. The incidence of cutaneous tuberculosis at the dermatology department of the University of Mexico City was 2.6 per cent. of all cases requiring consultation with a dermatologist, according to ESTRADA. In a report on 50 000 cases of skin disease at the Out Patient Department of the School of Tropical Medicine in Calcutta, India, from 1942 to 1946 GHOSH reports that the incidence of skin tuberculosis was 0.5 per cent. (320 cases) There were 256 cases of tuberculosis verrucosa cutis 39 lupus vulgaris 22, scrofuloderma 3 erythema induratum Bazin, During the same 4 years, 903 cases of syphilis and 72 of oriental sore were observed

Our impression is that the incidence of cutaneous tuberculosis in inhabitants of the tropics and in the American Negro parallels, to a great extent, the infection rate of systemic tuberculosis in these groups. The incidence in the native population in tropical countries depends primarily on the opportunity for contact with infected members of other races and on the general distribution of the population. In Malaya, for instance we found very little cutaneous tuberculosis among the Malays living under rural conditions where the incidence of pulmonary tuberculosis also was very low There were more cases among Tamils living on rubber plantations where the incidence of pulmonary tuberculosis was higher The largest number of cases of cutaneous

tuberculosis was among Chinese residing in larger cities under crowded living conditions and the incidence of pulmonary tuberculosis was correspondingly high.

The same pattern of incidence of cutaneous tuberculosis is apparent in the American Negroes Eight times as many American Negroes as members of other races in America suffer from pulmonary tuberculosis. It is our impression from observations made in various clinics and in private practice in San Francisco that the infection rate of cutaneous tuberculosis in the Negro is about ten times higher than that in the other races, conforming approximately to the incidence of pulmonary tuberculosis in these two groups

CLASSIFICATION

Different basic approaches have been used by GANS, JADASSOHN and LEWANDOWSKY and others to classify cutaneous tuberculosis.
The following classification is based on whether the infection is primary or is a re-infection and on the morphology of the lesions

	Localized	*Disseminated*
Primary Infection	Inoculation tuberculosis Tuberculous chancre Primary tuberculous complex	Tuberculosis cutis miliaris acuta generalisata (of pulmonary or meningeal origin)
Re-infection	Lupus vulgaris Tuberculosis cutis luposa Tuberculosis cutis verrucosa Tuberculosis cutis colliquativa (scrofuloderma) Tuberculosis cutis orificialis	Lichen scrofulosorum (tuberculosis cutis lichenoides) Tuberculosis cutis papulo-necrotica Tuberculosis cutis follicularis disseminata Lupus miliaris disseminatus faciei (lupoid papular tuberculid) b. Micropapular tuberculid (rosacea-like tuberculid Lewandowsky) Tuberculosis cutis indurativa a. Erythema induratum Bazin (b. Lupus pernio c. Sarcoid Boeck miliary lupoid d. Sarcoid Darier Roussy)

MICHELSON and LAYMON considering that the onset of a tuberculoderma is very important because it characterizes all cases in a certain group and is due to certain unknown qualities in the patient's tissues, divided the disease first into two forms (1) stable forms, exemplified by lupus vulgaris, and (2) labile or transient forms, exemplified by the tuberculids From this classification they went further and used the prognosis of tuberculodermas as a basis for classification, subdividing some according to common characteristics. Although this classification does not help us as pathologists, it has practical clinical value and is certainly worth remembering

A. Forms which are chronic and progressive and rarely terminate fatally
   1 Tuberculosis cutis luposa. 2. Tuberculosis in the American Negro.
      3 Sarcoidosis

B Forms which tend to heal
   1 Relatively rapidly
      a Primary cutaneous tuberculous complex. b. Tuberculosis verrucosa cutis. c. Tuberculosis cutis lichenoides (lichenoid papular tuberculid). d. Tuberculosis cutis papulonecrotica (necrotic papular tuberculid)
   2. More slowly
      a. Tuberculosis colliquativa (scrofuloderma). b. Erythema induratum (necrotic nodular tuberculid). c. Tuberculosis miliaris disseminata faciei (lupoid papular tuberculid)

C. Forms which usually terminate fatally
   1 Tuberculosis cutis miliaris acuta generalisata. 2. Tuberculosis cutis orificialis

SYMPTOMATOLOGY

Lupus vulgaris is not frequently observed in inhabitants of tropical countries and in the American Negro It usually affects the face often originating from an infection of the nasal mucous membranes. The elementary unit is the lupus nodule which may begin as a small red or black macule It is usually described as apple-jelly-like in consistency and colour and best demonstrated by diascopic pressure. Diverse arrangement of such lupus nodules combined with hypertrophy ulceration, crusting and scarring create a great variety of clinical forms identified by adding descriptive adjectives to lupus vulgaris tumidus hypertrophicus psoriasiformis, *serpiginosus*, *profundus* gangrenosus vegetans mutilans, etc.

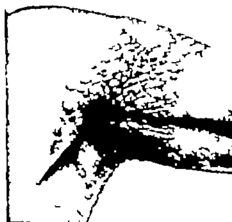
In the differential diagnosis cutaneous leishmaniasis, deep mycoses

and syphilis are important possibilities. The recidivous nodules in the scar within the serpiginous borders are helpful in the diagnosis of lupus vulgaris.

Tuberculosis verrucosa cutis starts as a papulopustule at the site of in-



465 Lupus vulgaris.
(Scull-Chicago)



466. Lupus vulgaris.
(Scull-Chicago)

See references at the end of this chapter



467 Lupus verrucosus of the planta pedis.



468 Tuberculosis verrucosa cutis in a Japanese
(Letterman Army Hosp Phot Lab – San Francisco)

fection and later becomes a verrucous lesion. It affects most frequently the extremities, usually hands, feet and ankles and most commonly occurs in persons who by their work are exposed to infection with the tubercle bacillus The so-called *anatomical tubercle* or *verruca necrogenica*, an example of this type of infection, was relatively frequent in pathologists and their helpers in the past when dissecting was done without gloves People handling cattle or working in slaughterhouses are more likely to have tuberculosis verrucosa cutis caused by the bovine type of tubercle bacillus. Tuberculosis verrucosa cutis is the type of



469–470 Tuberculosis verrucosa cutis
(*Scull—Chicago*)

cutaneous tuberculosis one most frequently encounters in tropical countries, but not so frequently in the American Negro.

In the differential diagnosis the deep mycoses, especially blastomycosis and chromoblastomycosis and bromoderma must be considered.

Tuberculosis colliquativa or *scrofuloderma* is relatively frequent in tropical countries and also in the American Negro It commonly affects the neck and trunk, but may be found on the buttocks. It originates from underlying structures, usually infected lymph nodes bones and joints The lesion begins as a nodule which softens in the centre. Soon

the nodule breaks open, and thin purulent exudate mixed with caseous material and blood escapes Sinuses form and later ulcers with irregular borders develop and in the end stages healing produces retracted scars

Tuberculosis cutis orificialis is characterized by indolent, shallow ulcers around the mouth or anus of persons suffering from laryngeal pulmonary or intestinal tuberculosis This form occurs in tropical countries and in the American Negro whenever systemic tuberculosis is prevalent.

Of the disseminated forms, *tuberculosis miliaris acuta generalisata* a



4 1 T berculosis of the right eye and lacrimal duct
(*Scull-Chicago*)

usually fatal disease, is seen mainly in children. It results from dissemination of systemic tuberculosis (pulmonary meningeal, postexanthematic) Fortunately it is a rare form. The skin lesions, which may be macular papular vesicular or pruritic, abound with tubercle bacilli.

Lichen scrofulosorum (tuberculosis cutis lichenoides) is characterized by flat lichenoid papules which are occasionally slightly scaly and occur on the trunk Contrary to the statement frequently found in the literature that lichen scrofulosorum is rare in tropical countries and among the American Negroes it is our impression that it occurs not infrequently but that its presence is often not recognized in dark-skinned

persons. We have seen a number of cases among Tamils, Chinese, Mexicans and Japanese and also among American Negroes. It is a benign haematogenous infection which heals slowly without scar formation

Papulonecrotic tuberculids occur in the American Negro, but seem to be uncommon in natives of tropical countries. Lesions are present on the face and extremities and occasionally on the trunk. This form is also called *acnitis* when the distribution of the lesions is limited to the face and *folliclis* when the distribution is limited to the extremities It is



472. Tuberculosis colliquativa in a Negro.

believed that bacilli are disseminated via the circulatory system and lodge in these tissues producing lesions characterized by central necrosis and scar formation.

Syphilis, drug eruptions and acne necroticans should be considered in the differential diagnosis.

Tuberculosis miliaris disseminata faciei also called *lupus miliaris disseminatus faciei* is a haematogenous tuberculosis not uncommon in the Negro population of America. It is characterized by red-to-brown, pin head-sized or larger papules. A brownish colour remains on diascopic pressure The lesions tend to spontaneous remissions. The tuberculin test in this type of infection is almost negative for reasons which

are not clear It is rare in the tropics. In 10 cases of disseminated cutaneous tuberculosis observed in Negroes by KETRON and GINSBURG the lesions varied from small lichenoid papules to irregular infiltrations. The majority had a lupus miliaris faciei type of reaction and only 3 had lesions of sarcoid like structure.

An eruption affecting the face, especially the cheeks and forehead, consisting of bluish red papules and pustules is known as *rosacea-like tuberculid* (LEWANDOWSKY). MICHELSON and LAYMON suggested the name *micropapular tuberculid* It is a rather controversial entity not seen



473 Tuberculosis colliquativa which was cured by tubercazon therapy
(Simon Amsterdam)

in tropical countries IRGANG stated that micropapular tuberculid occurs frequently in the American Negro and has a distinctive clinical appearance not resembling rosacea. He described firm, discrete clinically non inflammatory papules that tended to regress relatively rapidly leaving slightly depigmented areas and occasionally depressed scars Lesions were located most commonly on the face and there was no involvement of the canthi alae nasi or vermillion border of the lips areas characteristically involved by tuberculosis miliaris disseminatus faciei

A special form of haematogenous tuberculosis of the skin, *erythema*

Induratum Bazin is usually located on the flexor surfaces of the legs. The deep-seated nodules often ulcerate. Women are more frequently affected than men. This form is observed rather frequently in the American Negro in whom it may resemble erythema nodosum with an atypical distrubution of the lesions It presents numerous differential diagnostic problems. Gumma, nodular vasculitis and nodular nonsuppurative panniculitis must be considered. In the tropics, deep mycoses and leprosy add to the diagnostic difficulties.

Tuberculosis in the American Negro includes a group of cases of debatable aetiology and classification. KLAUDER, KLAUDER and WEIDMAN KETRON and GINSBURG and others have described a distinctive syndrome occurring in the American Negro which is probably a sarcoid like tuberculosis. THOMAS added 12 cases to the literature and the distinguished five types (1) a superficial erythematous variety affecting scalp and face, resembling lupus erythematosus, (2) grouped and scattered superficial nodules, (3) brownish-red, indurated plaques of various sizes assuming annular configuration, (4) nodular-ulcerative lesions of the legs, resembling erythema induratum, (5) cherry-sized to walnut-sized subcutaneous nodules.

PATHOLOGY

The interest of the dermatopathologist in diagnosing, if possible the specific form of cutaneous tuberculosis is not only academic a correct diagnosis has considerable practical value in determining the therapeutic approach and the prognosis.

The following points are important in the diagnosis of the various forms of cutaneous tuberculosis (1) localization of pathological changes, (2) presence or absence of caseation, (3) cytological changes, (4) presence or absence of tubercle bacilli.

The fundamental pathological unit is the tubercle. In its complete form it consists of an area of central caseation, Langhans giant cells, epithelioid cells, lymphocytes and at times also plasma cells However all of these elements are not always present but epithelioid cells are invariably present. Giant cells, if present, are more often of the Langhans type, with numerous nuclei arranged horseshoe like in the periphery of the group of epithelioid cells or they may form broad bands Plasma cells may surround the tubercle like a shell. Caseation is one of the most important criteria for the classification of cutaneous tuber

culosis and is much more frequent in cutaneous tuberculosis of tropical countries and in the American Negro than in other races

Lupus vulgaris The histopathological picture of the clinical unit, the lupus nodule, is a conglomeration of tubercles consisting of epithelioid cells and lymphocytes. Langhans giant cells are not always present, but if a large number of sections of the same lesion are examined, some *Langhans giant cells will always be found. Caseation is always* absent. Bacilli are difficult to find.

Tuberculosis verrucosa cutis The epidermal changes predominate, with marked hyperkeratosis, papillomatosis epidermal abscesses and



474 Histology of lupus vulgaris.

acanthosis producing pseudoepitheliomatous hyperplasia. In the corium there is a tuberculoid infiltrate consisting of epithelioid cells, Langhans giant cells lymphocytes and occasionally plasma cells Caseation can occur but is not always present. Bacilli are sometimes demonstrable and results of animal inoculation may be positive. The lesions greatly resemble those of North American blastomycosis and chromoblastomycosis, but in the latter two, giant cells are more numerous. Identification of the causative organism settles the differential diagnostic problem

Tuberculosis colliquativa or scrofuloderma This condition is characterized by marked caseation, formation of large abscesses and typical ab-

scesses in the periphery with caseation, epithelioid cells, giant cells, lymphocytes and numerous plasma cells. Tubercle bacilli are present. It is important to select the proper site in the lesion for taking a specimen for biopsy one may find only a plasma cell inflammatory infiltrate without characteristic structure in some areas.

Tuberculosis orificialis This clinical entity presents a variety of histopathological pictures, depending on the virulence of the infection and the resistance of the individual Frequently ulceration with caseation necrosis and tubercle formation can be seen. Tubercle bacilli are always present.



475. Histology of Lichen scrofulosorum.

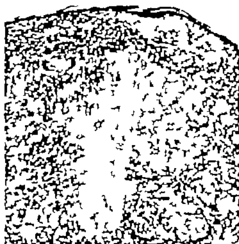
Tuberculosis cutis miliaris acuta generalisata This shows, occasionally tuberculoid structure, but more often only uncharacteristic granulation tissue with central necrosis. Many bacilli are present.

Tuberculosis cutis lichenoides or lichen scrofulosorum The most characteristic histopathological picture is seen in this form of cutaneous tuberculosis. In the upper corium, a minute tubercle consisting of epithelioid cells, lymphocytes and isolated giant cells is glued to the epidermis. It may but does not necessarily show a follicular location. In lichen nitidus, not a form of skin tuberculosis, a similar formation consisting of epithelioid cells and lymphocytes is found, but the arrangement does not form a tubercle

Lupus miliaris disseminatus faciei This is a superficial process and in early stages a collection of epithelioid cells surrounded by a mild lymphocytic reaction is the usual finding Later typical tubercles form which undergo central caseation.

Tuberculosis cutis papulo-necrotica or papulo-necrotic tuberculid. A central area of necrosis, reaching from the epidermis in a wedge-shaped form through the corium, is the characteristic finding The V-shaped, crusted necrotic areas are surrounded by tubercles. In the depth of the lesion one can find obliterative endarteritis and endophlebitis.

Tuberculosis cutis indurativa or erythema induratum Bazin. This con-



476. Histology of papulo-necrotic tuberculid

dition affects mainly the subcutis and usually the cellular picture is rather impressive. The changes in the subcutis range from a tuberculoid infiltrate consisting of groups of epithelioid cells and a few lymphocytes to typical tubercles with all constituents and marked caseation. Vascular changes are characteristic, a feature which at times may make the differential diagnosis between erythema induratum Bazin and gumma difficult. Of some help in this dilemma are the foreign body giant cells which together with Langhans giant cells, are present in syphilis in tuberculosis, Langhans giant cells predominate. In tuberculosis the vascular changes are limited to the affected areas whereas in syphilis vascular changes can also be seen in the

surrounding tissue. Erythema induratum Bazin has certain histopathological similarities to papula necrotic tuberculid. A differential diagnostic problem is presented by leprosy especially the diffuse form of the lepromatous type.

Inoculation tuberculosis or primary cutaneous tuberculous complex In the early stage there is only an uncharacteristic inflammatory infiltrate con-consisting of polymorphonuclear leukocytes, lymphocytes and a few plasma cells, and some necrosis. Tubercle bacilli are numerous. Later, typical tubercles form with central caseation, epithelioid cells, giant cells and lymphocytes, and on the periphery plasma cells. As these changes take place the tubercle bacilli become less numerous.

DIAGNOSIS

The clinical diagnosis of cutaneous tuberculosis should be substantiated by laboratory work whenever feasible because even with great experience it is possible to mistake other diseases for tuberculosis. The following must be especially considered in the differential diagnosis deep mycoses syphilis, bromo- and iodo-derma, malignant lesions granuloma inguinale and cutaneous leishmaniasis.

The difficulty in the clinical diagnosis of tuberculosis of the skin is increased in dark skinned people by the fact that the important criteria of colour of the lesion, as well as the colour change on diascopic pressure are much more difficult to see and therefore have much less diagnostic value The clinical picture can be further complicated, especially in tropical countries, by the simultaneous occurrence of several diseases in the same person.

The demonstration of tubercle bacilli in smears from skin lesions is successful only in certain forms of cutaneous tuberculosis and is unsuccessful in many cases. The same is true of animal inoculation performed on guinea pigs. It gives more positive results than examination of smears, but is negative in many forms of cutaneous tuberculosis.

The tuberculin test, an expression of the state of allergy of the individual, can be of great help in distinguishing between the various forms of cutaneous tuberculosis but is of very limited diagnostic significance.

The most important diagnostic method is histopathological examination Presence of Mycobacterium tuberculosis in the sections is of

course diagnostic. If bacilli cannot be detected it is sometimes possible to make a definite diagnosis on the basis of the histopathological picture alone as it is in lichen scrofulosorum or in tuberculosis verrucosa cutis However in some cases it is necessary to correlate clinical appearance, histopathology and reaction to tuberculin in order to arrive at the correct diagnosis.

THERAPY

Local treatment of cutaneous tuberculosis was of great importance before the advent of systemic therapy For lupus vulgaris application of 10 per cent pyrogallol ointment and irradiation with the Finsen lamp were valuable methods In tuberculosis verrucosa cutis excision is an excellent method if the size and location of the lesion are suitable and promise a good functional and cosmetic result. Scrofuloderma occasionally warrants incision or excision and X-ray treatment Promin-jelly is sometimes useful in the treatment of scrofuloderma. In tuberculosis cutis orificialis and in the so-called tuberculids, no special local therapy is successful.

The *systemic therapy* of skin tuberculosis became successful for the first time when CHARPY introduced treatment with large doses of calciferol (vitamin D_2) *Calciferol* is given in weekly doses of 600,000 units either in a single dose per week, or distributed in four doses of 150 000 units each. Early in treatment, larger doses are suggested 600 000 units three times in the first week and 600 000 units two times a week in the following three weeks Additional administration of *streptomycin dihydrochloride* in daily doses of 0 5 to 1 g is valuable. In some forms of cutaneous tuberculosis for example in tuberculosis verrucosa cutis local injection of streptomycin in procaine solution gives excellent results *Para-aminosalicylic acid* by mouth in doses of 8 to 12 g daily either alone or with streptomycin, has been reported successful. The *thiosemicarbazones* are under trial.

SARCOIDOSIS

This disease has been described under different titles by different authors BESNIER in 1889 described nodular reddish blue lesions of the face nose and fingers under the title "*lupus pernio*" HUTCHINSON had described a case of similar lesions in 1875 The term *sarcoid* was first used by BOECK in 1899 when he reported a case in which there

were large infiltrated plaques. DARIER and ROUSSY in 1906 described nodular subcutaneous tumours. In 1909 HEERFORDT reported the syndrome of *uveoparotid fever*. Osseous lesions were described by JUNGLING in 1919 as *ostitis tuberculosa cystoides*. In several publications SCHAUMANN correlated these various clinical manifestations into a single systemic disease which he called *lymphogranulomatosis benigna*.

DEFINITION

The following definition of sarcoidosis was adopted by the Conference



477 Benign lymphogranulomatosis with [illegible]

(Scull-Chicago)

on Sarcoid of the National Research Council in Washington on February 11 1948:

Sarcoidosis is a disease of unknown aetiology. Pathologically it is characterized by the presence in any organ or tissue of epithelioid cell tubercles with inconspicuous or no necrosis and by the frequent presence of refractile or apparently calcified bodies in the giant cells of the tubercles. The characteristic lesions may be replaced by fibrosis, hyalinization or both.

Clinically the lesions may be widely disseminated. The tissues most frequently involved are lymph nodes, lungs, skin, eyes and bones

particularly of the extremities – The clinical course usually is chronic with minimal or no constitutional symptoms however there may be acute phases characterized by a general reaction with malaise and fever There may be signs and symptoms referable to the tissues and organs involved. – The intracutaneous tuberculin test is frequently negative the plasma globulins are often increased. – The outcome may be clinical recovery with radiographic evidence of residue, or impairment of function of organs involved, or a continued chronic course of the disease."

It is well established that a local sarcoid reaction may be a response to various stimuli such as silica and tattoo pigment. *Sarcoidosis like lesions may develop in an occasional otherwise typical case of certain diseases including tuberculosis syphilis and leprosy* By definition these cases are excluded from the clinical diagnostic entity sarcoidosis. In addition, the distinctive syndrome in the American Negro described by KLAUDER KLAUDER and WEIDMAN THOMAS, KETRON and GINSBERG and others is excluded because it is probably a sarcoid like tuberculosis.

AETIOLOGY

Many theories have been advanced concerning the cause of sarcoidosis but the issue remains unsettled. JADASSOHN MARTENSTEIN and PINNER felt that sarcoidosis is a form of tuberculosis. CURTIS and others have stated that it is not an aetiological entity and may be produced by a wide variety of stimuli PAUTRIER felt that the disease is a reticulo-endotheliosis not a granulomatous and not necessarily of infectious origin MICHELSON regarded it as a specific entity produced by a single specific aetiological agent. In an extensive review of the aetiological concept of sarcoidosis ROSTENBERG concluded that the most likely cause is a new infectious agent.

EPIDEMIOLOGY

Sarcoidosis is a clinical entity which occurs throughout the world in all races both sexes and in any age group The geographic distribution of sarcoidosis does not coincide with that of tuberculosis and the disease may occur in the apparent absence of exposure to tuberculous individuals Sarcoidosis occurs predominantly in rural areas while tuberculosis is most prevalent in urban areas While sarcoidosis seldom affects the inhabitants of tropical areas it is especially common in the

American Negro particularly those residing in the southeast section of the United States

So far as is known, man to man transmission of sarcoidosis does not occur No animal reservoirs of the diseases are known to exist. The disease rarely affects more than one member of a family and most patients with sarcoidosis have not been in intimate contact with another patient affected by sarcoidosis.

SYMPTOMATOLOGY

Sarcoidosis, a generalized disease may involve any organ in the



478. Sarcoidosis.

(Scull-Chicago)

body Those most frequently affected are, in order *lymph nodes lungs skin eyes and bones* A great variety of signs and symptoms may be noted, depending on the organs involved, or there may be complete lack of symptoms despite widespread involvement of many organs. In addition to symptoms referable to the various organs a patient with sarcoidosis may experience weakness and fatiguability anorexia, pains in the joints dyspnoea, cough and chest pain, low-grade fever and weight loss.

The lymphatic system the one most frequently involved, is affected in most cases. A single node may be affected or involvement may be

widespread. The nodes may become palpable and even look like tumours under the skin. This is the presenting symptom in some cases. The nodes are firm, usually discrete and non-tender. The spleen and less frequently the liver may be enlarged. Hodgkin's disease, leukaemia and other lymphomas must be considered in the differential diagnosis of these findings.

The lungs are next most frequently the site of this disease. They may be affected either with or without involvement of the bronchial lymph nodes. Physical signs and symptoms may be minimal or absent in spite of widespread distribution shown by roentgenological examination.



479 Sarcoidosis.
(Szell-Chicago)

The roentgenological appearance varies from a diffuse increase in linear markings and fibrotic infiltrations to multiple nodular densities in addition to enlargement of the hilar lymph nodes.

There are *skin lesions* in approximately 50 per cent. of cases of sarcoidosis. These are usually divided into three groups. The group classified as Boeck's *sarcoid* are round, oval or irregular-shaped papules, nodules and plaques. They may be few or widespread. Their colour varies from red to purple with occasional brownish yellow areas. Occasionally peripheral scaling and telangiectasia are found. The lesions are most

often found on the extensor surfaces of the arms and on the face. The second group called *lupus pernio* of BESNIER, are characterized by symmetrical large infiltrated plaques with indistinct margins, bluish red, and occurring on the *nose, ears, fingers, face and less frequently* on the hands, feet and toes In DARIER ROUSSY *sarcoid* the third group, are the lesions of the subcutaneous tissue of the extremities, trunk and face. They are usually round or oval and vary in size from 1 to 3 cm. The colour of the lesions may vary from that of the normal skin to pink to dull red. MICHELSON has emphasized that almost every kind of cutaneous change can occur in sarcoidosis. He stressed the



480. Sarcoidosis multiple hyperkeratotic lesions.
(Scull-Chicago)

polymorphic appearance of the lesions and stated that instead of the usual classifications and terms, descriptive terms such as papular cutaneous sarcoid should be used. Atypical skin lesions resembling granuloma annulare acrodermatitis chronica atrophicans and lupus erythematosus have been described *Erythroderma* and verrucous lesions have also been described. *Erythema nodosum* may occasionally be the first symptom of the disease

Sarcoidosis involves the *eyes* in from 30–40 per cent. of the cases. Dimness of vision is the most common symptom. Painless iridocyclitis, "mutton-fat"

type keratitic precipitates, nodules on the iris and rarely involvement of the lids and retina may occur according to LEWIS. *Uveoparotid fever* of HEERFORDT is a syndrome of iritis or iridocyclitis accompanied by enlargement of the parotid and occasionally other salivary glands produced by sarcoidosis. By bilateral involvement of the lacrimal and salivary glands sarcoidosis may produce the picture of MIKULICZ *syndrome*.

JÜNGLING described *sarcoidosis of the bones* under the title osteitis tuberculosa multiplex cystica. Bony changes occur in 10–20 per cent. of patients with sarcoidosis. Fusiform swellings of the phalanges is the most common symptom, while joint pain and stiffness are rare. Bony lesions may be apparent in roentgenograms as either circumscribed circular areas of rarefaction or diffuse reticulated small areas of rarefaction. Osteoporosis peri-articular soft tissue swelling and cartilage destruction are rare. In addition to the lesions just described, any organ of the body may occasionally be the site of sarcoidosis.

PATHOLOGY

The characteristic lesion of sarcoidosis is a discrete granuloma com-



481 Histology of Boeck's sarcoid.

posed of epithelioid cells sharply delimited from the surrounding tissue with few lymphocytes and fibroblasts at the margin as described by RICKER and CLARK in their recent review. The epithelioid cells are uniform, polyhedral cells with abundant acidophilic cytoplasm and large ovoid and vesicular nuclei. As lesions regress they are replaced by fibrous tissue. Central necrosis and caseation are usually

absent. Giant cells of the Langhans type may be present, usually in small numbers. Inclusion bodies may appear either intracellularly or extracellularly. *Asteroid inclusion bodies* present in giant cells, are often seen in sarcoid, but are not specific for this condition. The epithelioid tubercles are most frequently seen grouped around the small blood vessels. Lesions in the lymph node do not involve the capsule. Differential diagnosis must include tuberculoid leprosy, foreign-body granuloma from silica or beryllium and tuberculosis. It is often extremely



482. Histology of sarcoid Darier Roussy



483. Sarcoid. Asteroid bodies in giant cells.

difficult to distinguish sarcoidosis from leprosy and tuberculosis. In addition, often it is not easy to decide how much caseation, how many giant cells and how many lymphocytes are compatible with the diagnosis of sarcoidosis. The similarity of the histopathological picture in conditions caused by widely different aetiological agents—syphilis, tuberculosis, leprosy, leishmaniasis, deep mycoses, as well as various foreign-body granulomas suggests strongly that sarcoidosis is only a tissue response in a peculiar state of immunity.

LABORATORY FINDINGS

The results of routine blood studies are usually within the normal range. A mild anaemia may be found occasionally and the leukocyte count may be at the lower limits of normal. *Eosinophilia* has been re



484 Boeck's sarcoid
(Carol Amsterdam)

ported, but is present infrequently HARRELL described transient monocytosis

Changes in the serum protein are a characteristic finding first described by SALVESEN The *globulin fraction* is increased markedly the total protein level is elevated and the albumin-globulin ratio is revers-

ed. *Hypercalcaemia* is a relatively frequent finding. CURTIS found elevated non-protein nitrogen and serum phosphorus and decreased urea clearance.

The results of examination of the *urine* are usually normal.

Failure of patients with sarcoidosis to react to tuberculin has long been considered characteristic of the disease. However some patients



485. Boeck's sarcoidosis initially taken for tuberculoid leprosy

(Vrijman-The Hague)

with sarcoidosis have had a positive tuberculin reaction. This finding of anergy to tuberculin has been discussed at length by ROSTENBERG.

The KVEIM *intracutaneous test* has recently been the subject of study by DANBOLDT, LEIDER and NELSON. It consists of the intradermal injection of 0.1 ml of an extract prepared from lymph nodes involved by sarcoidosis or from normal spleen extracts. A positive result, manifest in a papular response, occurs in from 2 to 3 weeks in cases of active sar

coidosis DANBOLT and others feel that the test is of diagnostic significance LEIDER and NELSON feel that it is not a diagnostic measure, but may be of prognostic significance.



486 Nodular form of Boeck's sarcoid called angiolupoid (because of its histology) in a Eurasian girl.

(Siemens Leyden)

PROGNOSIS

The lesions of sarcoidosis are usually chronic and tend to heal slowly They may persist indefinitely or clear spontaneously with minimal scarring While repeated exacerbations and remissions occur in most cases, the disease regresses completely in approximately 25 per cent. of the cases Death may occur as the result of the involvement of vital organs or from intercurrent infection, usually tuberculosis. Blindness rarely results from ocular involvement. In general the prognosis in sarcoidosis is good so far as life expectancy is concerned but poor in regard to complete regression of the disease. The disease is somewhat more severe in the American Negro than in other races.

THERAPY

There is no uniformly successful treatment for sarcoidosis available at this time In the past many therapeutic modalities have been used

with little therapeutic effect. The early favourable reports of the use of arsenic have not been substantiated by recent observations. Recent interest in treatment has centered around calciferol, cortisone and adrenocorticotropic hormone. Although some reports have been favourable, these agents leave much to be desired in the treatment of sarcoidosis

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CHAPTER 21

CUTANEOUS PLAGUE

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DEFINITION

As a direct result of infection of the skin with plague, affections of the skin may occur in the course of any type of the disease. The frequency of such lesions seems to vary with different epidemics hence some authors are inclined to regard cutaneous plague as a seperate clinical entity They classify as such those cases which are characterised by skin lesions either at once or at an early stage, but without buboes. Most authors do not share this opinion. They distinguish a cutaneous plague, in which cutaneous lesions play a prominent part, but they consider these as secondary complications. Whether these will appear or not, is a matter of time. In such a rapidly fatal disease there is usually no time for complications the patient does not live long enough to develop cutaneous lesions. Hence skin affections are seldom, if ever mentioned in descriptions of the most fulminant type pneumonic plague. Clinically and pathologically therefore the classical division into *bubonic septicaemic* and *pneumonic plague* is maintained.

HISTORY

Whether all the diseases designated in ancient times as pestis or "pestilentia" correspond with our present clinical entity may be questioned In general, epidemic diseases with a high mortality rate were meant by these terms.

In the Old Testament (I SAMUEL, 5 and 6) plague is described as a "deadly destruction" from which people "without number" died and which was attended by "emerods in their secret parts" It is remarkable that plague is spoken of in the same breath with the rat, for the afflicted Philistines were advised to placate the wrathful God of Israel, by making images of the emerods and of the rats. Perhaps at that time



487 Large plague ulcer with marked adenitis in the neck.

plague and the rat were felt to be obscurely linked, a link which has become definitely established only in our time.

In the Middle Ages Europe was visited by a pandemic which, in extent and violence has never been equalled in history Though smaller in size, many other epidemics followed this great pandemic of the 14th century until finally the plague lost its grip on Europe at the end of the 17th century Why the name of "*black death*" came into vogue in the Middle Ages is not quite clear Some of the skin affections, to be described more precisely below are supposed to have given rise to this name But in that case they should have been much more frequent

and extensive and—as is possible because of the paleness of the skin of the white races—much more striking than we commonly note in the Oriental races In this connection it may be interesting to quote one of the oldest morbid anatomical descriptions of plague, eg that by GEORGE THOMSON, M D who carried out an autopsy during the great plague of London in 1666 He writes "the head of the coffin being taken off and the linen cleared away I could not but admire to behold a skin, so beset with spots black and blew more remarkable for multitude and magnitude, than any I have yet seen some of which being opened, contained a congealed matter in one more shallow and in another more deep"

EPIDEMIOLOGY

Until the middle of the 19th century serious epidemics still occurred occasionally in Europe, but they did not spread over large areas, whereas Western Europe was spared for the greater part after the end of the 17th century Even in our time, however the danger is not over as is proved *e g* by the small epidemic of 1920 in Paris among the rag pickers living in the basements. Towards the end of the 19th century the plague began to spread from Hongkong over Eastern Asia and from there over a great part of the world. Egypt and Japan were reached at about the same time then the Philippines and South America were invaded. Only much later Ceylon followed and in 1911 Java, where the disease swept in great waves from East to West India also has suffered heavily from the plague with a mortality of ten million-odd in twenty years *The principal endemic centres are nowadays* Manchuria and Eastern Siberia with pneumonic plague chiefly and China, Indo-China, Siam, Java, India Iraq Northern Africa and Nigeria, Uganda, Kenya, the Eastern part of the Belgian Congo Madagascar and South Africa, and California to some extent with the so-called sylvatic plague —the ground squirrel being the intermediate host there— and certain parts of South America such as Peru Ecuador Chile, Brazil and the Argentine

AETIOLOGY

The specific cause of plague is the Bacillus or *Pasteurella pestis* dis

covered by Yersin in 1894 during an epidemic in Hongkong *Pasteurella pestis* in its typical form is a thick, short, non-motile bacillus of a length of 1—2 μ, which is easily stained with aniline stains it is Gram-negative It stains more vividly at both rounded ends, showing a bipolar con figuration in the stained preparation. A characteristic feature is its *polymorphism* short forms resembling diplococci alternate with more slender rods This distinguishes them from putre-



488 Papules of cutaneous plague surrounded by erythema.
(Snijders–Amsterdam)

factive organisms, which may be found in dead material, but which are more uniform.

The plague is transmitted by the rat flea, *Xenopsylla cheopis* There are more species of rat fleas. Experimental infection with plague of the Pulex irritans has also been successful. Besides the rat other rodents may act as host, *e.g.* the ground-squirrel (which is responsible for sylvatic plague as already stated) The *rat flea-man theory* being drawn up first and established experimentally in 1898 by Simond was definitely proved and generally accepted in 1905 By that time the epidemiology

of the plague had become clear *Human plague is always preceded by rodent plague* Only when the mortality of the rats has become high and the rat fleas leaving their dead hosts, cannot easily find a new host, do they attack man. Everywhere close contact between man and rat may result in infection in this way

Pneumonic plague may occur secondarily in every psyllogenous plague (transmitted by the rat flea) These cases in turn may lead to the occurrence of an explosion, or if circumstances are favourable, to an epidemic of primary pneumonic plague, which may spread in



489 Cutaneous plague. Note miserable physionomy of the patient.

dependently without the rat flea, as vector from man to man, by *aerogenous infection*

These epidemics of pneumonic plague occur in cold climates only as for example the notorious epidemic of 1911 in Manchuria, which broke out in winter and caused an enormous mortality among the closely crowded population. As pneumonic plague has no dermatological importance because of its lightning course it will not be considered here again.

Infection by the rat flea takes place during blood-sucking Owing to a peculiar mechanism, blood, containing bacilli is regurgitated

from the fore-stomach of the flea, which becomes congested when the blood does not flow off sufficiently to the stomach. Via the opened skin capillary the bloodstream of the victim will be infected directly with plague bacilli. In treatises the opinion most often held is that a primary lesion arises at the site of the flea bite. From there the regional lymph nodes become infected through the lymphatics and thus the *primary bubo* arises. Only after a break through of this barrier would *septicaemia* arise. I should like to point out the fact that skin affections, which might be regarded as at all primary lesions, are hardly ever found. Also a *lymphangitis* leading towards a regional



490 Wide spread and deep necrosis in a patient suffering from plague

bubo is never seen. There is little reason, as will be explained below in more detail, to regard this as the usual course of events.

At any rate plague bacilli may already be cultivated from the blood in the first days of the disease. This holds good as well for the so-called septicaemic plague as for the bubonic plague. *There is therefore no fundamental difference between the two forms. Incubation* varies from three to five up to ten days. The latter period is observed accordingly for quarantine of contacts.

SYMPTOMATOLOGY

When judging the skin changes of a plague patient, they should be divided into *those certainly caused*, and *those not certainly caused* by the direct action of the plague bacillus. Plague patients are often very restless, rise from their bed, fall and bruise themselves. When purpura and even large blood extravasations are observed one should keep this



491 The former patient after cure.

in mind. Further there is the habit—a very widespread one in the East—of scarification of the face breast and back, by means of the rim of a coin They may as loci minoris resistentiae become infected by the plague bacilli There are also mosquito-bites, which are difficult to distinguish from the petechiae or small roseolae of plague. Often

only a histiological examination will give certainty as to the nature of these changes.

Full descriptions of the several skin affections are rare and rather divergent as now one kind predominates, now another This can be attributed partly to the fact that the skin affections undergo changes in form they develop from one stage to another Owing to the rapidly fatal course of the disease this development may be broken off at any moment, so at an autopsy now one form is seen, now another During the course of the illness however this development may be observed in the few cases that survive. A small *pustular rash* may become an eruption which strikingly resembles smallpox *roseolae* and flat *haemorrhagic infiltrations* may change into *ulcers* a small ulcer may extend into a large necrotic centre or "*plague-carbuncle*"

This is the explanation of the divergence of the descriptions of the different skin changes, which, in reality are only the developmental stages of one and the same affection. This should be borne in mind when one wishes to give a description of the different forms of cutaneous plague. They may be summarized as follows

1 ROSEOLAE, mostly sparsely distributed, sometimes with the density of a scarlatina exanthema.
2. SKIN-HAEMORRHAGES, ranging from petechiae to larger ecchymoses, which may be found on any part of the body solitary or multiple FRANÇA stated that, in 1899 they were observed during the epidemic at Oporto neither in such density nor in such extension, to justify the name of "Black Death" They were seen 46 times in 110 autopsies
3 VESICULAR AND PUSTULAR RASHES. These may be very sparsely distributed over the body or densely The pustules may show the depressed centre characteristic of smallpox, but they appear in contrast to variola, more sparsely on the face than on the rest of the body FRANÇA saw only once in his six cases a marked infection of the face but apart from that, he admits that die Eruptionen denen der Blattern zum Verwechseln ähnlich waren" Vos, in Bandung once had three cases at the same time with a similar rash, that came to autopsy Two of them appeared to have suffered from smallpox (positive PAUL's test on rabbits cornea), while in the third case plague was diagnosed The

rabbit's eye, infected with the pus from a pustule of this third patient, showed a violent conjunctivitis caused by the plague bacillus. Mention should be made here of the *Viruela pestosa* or *plague smallpox*. This was first described in 1913 in Ecuador. It occurred on the sixth or seventh day of the disease, after an apparent improvement. In 1915 out of a total of 1630 cases of plague it



492. Umbilicated plague blister on the thigh.

was observed 57 times. The mortality was 91 %. FRANÇA also saw the pustular eruptions occur exclusively some days after the onset of the disease.

4. FLAT HAEMORRHAGIC INFILTRATIONS, above which there is a livid discoloration of the skin. They occur both as multiple and solitary lesions, and they may be reabsorbed without ulceration.

5. ULCERS OF PLAGUE CARBUNCLES. They are larger or smaller either

superficial or deep-seated ulcers, with strongly infiltrated edges, which form a more or less elevated solid wall, above which the epidermis is lifted off, sometimes in many small blisters. On the surrounding skin similar blisters may also be found. The centre of the ulcer is formed by a black necrotic slough. These ulcers may attain enormous dimensions, even to the size of the palm of the hand. They occur multiple as well as solitary the larger ones being mostly solitary and they may be accompanied by a pustular eruption. They may appear primarily as well as secondarily in the course of the disease. FRANÇA assumed that in seven of his eleven cases they were primary

The way an ulcer originates may be described as follows in the centre of a red or livid-coloured, somewhat elevated skin infiltration, a bulla arises, which is filled with a slightly haemorrhagic fluid. The infiltrated portion of the skin is usually surrounded by a pale anaemic areola. When the blister bursts, the floor becomes visible as a pale-coloured area. The inflammation now spreads in all directions, while the centre becomes necrotic.

FRANÇA describes a case, in which on the second day of the disease three "pemphigus bullae" arose on the inner side of the leg Two days later at autopsy two pemphigus bullae and one carbuncle were found in the same place The description of the histiological picture also makes it probable that these bullae are the same as those observed in the development of the ulcers. This is confirmed by the fact that one of the bullae had apparently already developed into a carbuncle.

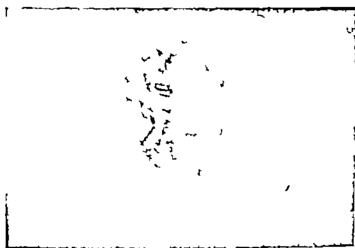
FRANÇA remarks moreover, that there is no circle of small vesicles around the carbuncle Thereby it could be distinguished from the anthrax carbuncle. We did, however, usually find them. A *regional bubo* may but need not, be present. Out of eleven solitary skin affections, most of them being ulcers or developing ulcers we found a regional bubo only six times. As opposed to the experiences of the German plague committee in Bombay and of FERRARI and GUIMARAES in Rio de Janeiro, FRANÇA found buboes in all cases with cutaneous plague.

The contingent occurrence of skin affections in septicaemic plague, without externally visible buboes should cause no surprise,

as they often arise secondarily probably by haematogenous spread. In our opinion there is no fundamental difference between septicaemic and bubonic plague, as in the former internal buboes may really occur or if the patient lives long enough, they may become visible externally in the course of the disease.

6 PERIADENITIS, in which the skin above the bubo is inflamed and adherent to it, usually develops very soon after the gland has been affected.

All surrounding tissues become affected by the inflammation, the



493 Collapse of blister in centre in a violet macule, which is again surrounded by a white area.

neighbouring groups of lymphatic glands sharing their fate. An extensive oedema forms which stretches far beyond the borders of the proper bubo over the trunk or the affected limb The covering skin, which is taut from the outset also becomes affected finally Oedema hard infiltration with bleb formation necrosis and ulceration follow in succession. The skin eventually ruptures when abscesses form The smaller buboes and those of a more benign character may be absorbed before the skin changes have become of a grave character

The *frequency* of the skin affections tends to vary in different epi

demics. In the morbid anatomical material of the former Netherlands Indies Cancer Institute it was 10 % in our clinical material, pertaining to the same epidemic in Java during 1929–1936 we found skin affections 18 times out of total of 251 cases *i.e.* 7 % (vaccinated patients not counted) Six of them were generalized, twelve were solitary affections. The former were all secondary and



494 Iliacal and femoral bubo of the right groin.

they occurred between the fourth and twelfth day of the disease Of the latter six were attended by regional bubo four out of these might be said to have begun with the skin affection, according to the patients history

If a pustule or a carbuncle is found associated with a regional bubo one is inclined to consider the latter as caused by the former Flu warned against this opinion. *Repeatedly carbuncles and other skin*

affections are seen to arise secondarily in the tributary region of a pre-existing bubo Still less do such findings justify the view that the carbuncle or the pustule should be regarded as a primary lesion at the site of the flea bite This erroneous supposition is all too frequently expressed.

Thus the German plague committee of Bombay described a series of cases with skin affections which they regarded as primary If we omit from these the case of one of the members of the committee, who infected himself during a post mortem, then four cases remain in which the skin affection is mentioned expressly as primary Considering the description of these cases, one should, however come to the conclusion that no evidence is produced that these are examples of a primary lesion.

Apart from the absence of bacteriological evidence of an existing plague infection, we sometimes find a history definitely pointing in another direction.

In one case, the course of which was fatal, a blister appeared on the ankle from the onset of the disease, with lymphangitis and a popliteal and a femoral bubo Fluid aspirated from the buboes was sterile, however

Only one case, which was observed from the beginning of the disease might be regarded as beginning with a primary lesion.

All things considered, it may be stated that while the skin forms the portal of entry *primary involvement of the skin is rare and primary lesions if they do occur are extremely exceptional*

Most authors therefore consider the skin affections as secondary Thus, *e g* CROWELL says

"The skin is frequent seat of secondary plague lesions and plague bacilli may also contaminate wounds and abrasions of the skin Therefore the presence of plague bacilli in cutaneous lesion, even though the infection occurs in the part of the skin drained by the glands constituting the primary bubo, is not sufficient evidence to class that lesion as indubitably the primary of entry"

The opinion has been advocated that the occurrence of skin affections justifies a favourable prognosis Probably this is based on a misconception. Skin affections generally occur rather late and so they are seen only when the patient remains alive long enough. But these are the cases which have a more favourable prognosis and which are

accessible to treatment. Some cases, observed by myself might illustrate the opinion given above

J J J a man, aged 31 was admitted to the clinic on Jan. 21 after having been ill for a day with fever and rigors. Two days later a tender gland was observed above the right clavicle, which, two days later again, showed a marked increase. Some painless glands were found, bilaterally below the mandible. On Jan. 25 the patient began to cough and bloody sputum was produced, in which plague bacilli were found. On Jan. 29 the patient was slightly icteric, and showed a papulo-pustular skin eruption on his breast, arms and thighs, which had spread the next day over the whole body the face included. The bubo decreased in size, but the general condition deteriorated. Death occurred on Febr 1st. In the contents of a blister plague bacilli were found. The blood culture (blood in bile) was positive on Jan. 21 26 and 29

A., a woman, aged 20 had been ill for two days before her arrival on April 2. In the right axilla a small tender gland was palpable, which ten days later developed into a bubo On April 11 pustules occurred on the limbs, becoming partly necrotic on April 16. Panophthalmia of one eye. Death on April 20 Blood culture positive.

A case of multiple, non-generalized infiltrations should be recorded separately:

A., girl aged 16, was sent in from a plantation where no plague had occurred. She had lived there for only five days, for three of which she had been ill. There was a bubo in the right groin (biopsy positive) with a lump above Poupart's ligament. After some days the epidermis was raised above the bubo like a bleb below this there was central necrosis of the skin. On April 17 a livid, tender infiltration of the skin the size of a penny occurred on the ulnar side of the left fore-arm two days later similar infiltrations arose on the left elbow left tibia and right thigh. No regional glands were swollen. Almost simultaneously corneal ulcers appeared on both eyes. The bubo ruptured and large necrotic masses were removed from it. After two months the patient had completely recovered, the skin infiltrations having been absorbed slowly without ulceration. The blood-culture was positive on April 11

The following case is illustrative of the question as to whether primary lesions occur or not. The patient was an intelligent man, who gave a detailed history

M., man of 30 had nursed his father for four days, who died from bubonic plague he was admitted quarantine-hut as a contact, being suspected of lung complications. On Jan 2 he discovered a small itching area on his forearm, which he considered to be mosquito-bite The next day pustule was seen there and in the evening he felt chilly On Jan. 4 he had marked temperature in the evening One day later the pustule had ruptured and showed enlargement. It was painful, but there was no bubo yet On that evening he discovered swollen glands of the arm and axilla On Jan 7 he was admitted to hospital. On the outside of the

forearm a penny-sized infiltration with central necrosis was to be seen. On the elevated wall some vesicles appeared. In the bicipital sulcus a diffuse swelling was seen, through which glands were palpable, further there was a pectoral bubo and a small gland in Mohrenheim's fossa. A stained preparation of the ulcer and the culture from the punctate were both positive. The blood culture was negative on Jan. 8 and 13. On Jan. 22 the patient was discharged as recovered after rupture of the bicipital bubo, and resorption of the other one.

The disease ran a mild course.

Such an extensive and reliable history is rare and we might conclude with some probability that there was a primary lesion at the site of the flea bite with a regional bubo and the progress of a local inflammation without septicaemia. If the area of itching had not occurred only three days after admission to the hutment. This pleads against it, unless one assumes the presence of infected fleas in the hutment.

Be this as it may, it shows once more how difficult it is in Oriental countries to form an opinion on such questions.

PATHOLOGY

Histologically the roseolae and the large extravasations present themselves as haemorrhagic infiltrations of the skin and subcutaneous tissue. The floor and the edges of the ulcers present on section a marked infiltration of the corium and the subcutaneous fatty and connective tissue, sometimes to a depth of several centimeters.

They are soaked with a purulent exudation and pervaded by haemorrhages. Microscopically, in addition to the haemorrhages considerable infiltration with polynuclear leukocytes and enormous masses of plague bacilli are found.

Between these there are degenerated or necrotic collagenic fibres. In the discharges of the bullae and the pustules and in the ulcers great numbers of the plague bacilli can be demonstrated.

One so finds in the skin also the intricate variegated picture of the haemorrhagic necrotizing inflammatory type of the plague, in other words the whole scale of changes brought about by the plague bacillus, though these may be studied best in the inflamed lymphatic glands. Some investigators feel authorized to indicate a certain skin change as a primary lesion, if this is solitary and accompanied by a regional bubo. Thus CROWELL described a papule on the dorsum of the foot with a femoral bubo at the same side, which might be con-

sidered as such, though he admits that the histological picture gives neither absolute certainty about it, nor excludes the possibility

Biopsy of the papule shows some oedema of the epithelial layer and the corium. In the corium and subjacent tissue the fibres of connective tissue are separated (oedema) The vessels are distended with blood. There are large masses of bacteria between the tissue fibres, about the sweat glands and the lymphatic vessels

A few polynuclear cells are present. There is a small haemorrhagic extravasation in the outer portion of the corium and some necrosis of tissue about this Nuclear fragments are scattered throughout the area. The area of involvement is greater in the subcutaneous tissue than in the epidermis the bacteria are very numerous and are present throughout the entire lesion. The endothelial cells lining the lymphatics are large and prominent"

In my opinion this description does not show such marked characteristics as to justify the classing of the papule as a primary lesion.

Among the autopsy material of the former Netherlands Indies Cancer Institute we found in 1938 out of a total of 187 post mortems 18 cases with skin affections

These had the character of solitary or multiple pustules, skin infiltrations, ulcers or larger necrotic areas, or they were more generalized as a vesicular bullous or pustular exanthema. Occasionally the changes were localized where the patient had had scarifications made on his breast or back with a coin, according to the habit mentioned above.

Around the infiltrations and pustules either an anaemic or a centrally red and peripherally pale areola was always found.

CLINICAL METHODS OF INVESTIGATION

For a conclusive diagnosis the only method is the bacteriological examination of the punctate from the buboes or the pustules and vesicles, of the discharges of ulcers and of the blood. In cutaneous plague this investigation will be simple in many cases. The contents of a pustule are smeared on a slide and stained with methylene blue or by GRAM's method.

FLU recommended that the air dried preparation be submerged in alcohol-ether and ignited before staining with LOEFFLER's methylene blue.

However the morphological picture may leave us in doubt, especially if putrefactive organisms are present, which might lead to confusion. The making of cultures therefore should never be omitted. Some times after culture in blood mixed with bile from a patient suspected of typhoid fever KIRSCHNER found plague bacilli instead of typhoid bacilli and investigated the value of bile in preliminary cultures. It appeared that bile mixed with small quantities of blood or pus gives, after inoculation even with only a few plague bacilli (10–40 per mil.), a good growth of these.

Moreover it is a great advantage, that bile checks the growth of staphylococci and streptococci which may be present in the pus of buboes or in pustules

With the aid of this selective blood-bile culture KIRSCHNER found, out of a series of 237 patients with clinically ascertained plague, a bacteriaemia in 90 % We obtained a positive result in 84 % of 127 patients in this way These figures are much higher than those obtained with the culture methods used previously With punctates of buboes the positive results of KIRSCHNER and of ourselves were 90 % and 80 % respectively In a certain percentage of cases in which cultures were made both from the blood and from the bubo punctate only one of them was positive It is therefore always essential to carry out both, as otherwise the diagnosis would miss its bacteriological confirmation in a small percentage of cases In practice the following procedure yielded good results from every patient suspected of plague. Blood is taken by venepuncture. This is diluted 1 to 2 or 3 times with bile and reserved for culture. Thereafter the bubo is punctured. Here the procedure should be as follows a not too thin needle is inserted swiftly while if necessary the glands are fixed. When the gland has been entered the point of the needle is moved to and fro several times then the needle is withdrawn slowly while aspiration is performed in this way some of the fluid out of the surrounding tissues is obtained in addition

Sometimes in this way some pus is obtained, sometimes only a little bloody fluid. Some drops of it are carefully pressed from the syringe on to a slide and a smear is made. The syringe is then rinsed by aspirating sterile bile a couple of times, and this is used for a culture. In

the same way the surrounding tissue of large ulcers or the contents of larger vesicles may be punctured.

Other clinical methods have only a relative value for diagnosis. The most valuable yet is the morphological blood examination In most cases a marked leukocytosis is found, the counts varying from day to day going up to 100 000. As a rule there is aneosinophilia, a marked polynucleosis many immature cells and a toxic granulation. But leukopenkia with relative lymphocytosis and aneosinophilia also occur which in the absence of buboes might suggest typhoid fever

PROGNOSIS

The prognosis of cutaneous plague is probably neither more nor less favourable than that of the plague in general, apart from primary pneumonic plague with its mortality of 100 / Because of the relatively small frequency of skin affections it is difficult to find data, which could be used statistically The mortality of the viruela pestosa which has been mentioned above, is given as 91 % without, however the mortality of this epidemic as a whole being mentioned.

DIAGNOSIS

After the preceding remarks on this subject in the foregoing pages we may be brief about differential diagnosis. The pustular eruptions may closely resemble smallpox, the plague carbuncle may resemble anthrax. The variegated picture of the different generalized affections of the skin may without being typical, force us to consider the possibility of all kinds of diseases which are accompanied by exanthemata or skin rashes and fever The presence of buboes and the general characteristics of the plague should put us on the right trail. The latter are blood-shot eyes a small rapid pulse a staggering gait, babbling speech and delirium. If buboes are absent and the general symptoms are not very marked the diagnosis at the bedside may be difficult.

Only bacteriological examination of the blood, of the punctate from a bubo and the discharges from the skin lesions may be able to provide certainty in such a case

It has to be pointed out that plague may occur in a very mitigated form in people vaccinated with the living vaccine. The patient walks around (pestis ambulans) or at least suffers little from the

disease (pestis minor) The possibility exists of an inguinal bubo being mistaken for an inguinal lymphogranuloma or for a syphilitic bubo. In regions where the plague is epidemic and vaccination has been carried out on a large scale, one should be on one's guard for this. In these mild cases the blood culture is usually negative and only the culture from the bubo is positive.

THERAPY

Treatment is chiefly directed against the disease itself. The local skin changes call for the usual measures such as the character of the affection may require

Up to recently the best results were obtained with *serum* This is prepared by injecting horses with increasing doses of virulent plague strains. It should be injected as early as possible and in large dosages. 20 to 40 ml are given, intravenously or intramuscularly if needed more is given.

The value of *sulphonamides* especially that of sulphadiazine, is now generally recognized. As a scheme for treatment the following is given most often initial dose 4 g then 1.5 to 2 g every 4 hours day and night, and without interruption, until the temperature has definitely become normal Thereafter a four hourly dose of 0.5 g should be continued for ten to fifteen days In the case of very delirious patients and in urgent cases the sodium salt is slowly given intravenously in a 5 % solution. The initial dose is 0 1 g per kg body weight, after that 0 06 to 0 1 g every four hours As soon as possible a change should be made to oral administration. The results are even a little better if sulphadiazine is combined with serum therapy

Penicillin has proved to be worthless *Streptomycin* on the contrary is active In cases in which sulphonamides fails, it may be life saving Even cases of primary pneumonic plague have been cured with streptomycin. After an initial dose of $^{2}/_{3}$ g a four hourly dose of $^{1}/_{3}$ to $^{2}/_{3}$ g should be given, as the gravity of the disease may require. The treatment should be continued until the patient is free from fever for 1–3 days Even higher dosages, up to 4 g daily have been given.

Aureomycin *chloromycetin* and *terramycin* seem also to be active as well *in vitro* as *in vivo*

Combinations of the preparations mentioned above are recommended.

PROPHYLAXIS

The only effective way of combatting the disease is to separate man and rat. This was achieved in Java by improving the houses of the population in such way that the rats could not make their nests there any more. This housing improvement, however takes a lot of time and in the meantime there are new victims. So there has always been a great need for a rapid prophylaxis For that purpose the Haffkine vaccine, prepared from killed cultures has been used for many years. With this vaccine the mortality could be reduced by 50 % at most. Much better results were obtained by Otten in 1935 with his living plague vaccine, prepared from the "Tjiwidej" strain, which had spontaneously become avirulent.

By the aid of this he was able to reduce the mortality after mass-vaccination of the most heavily infested districts of Java to 16 % of the mortality prevailing before the vaccination.

When nursing plague patients the strictest precautions should be taken. In the course of every case of plague, lung complications may occur quite unexpectedly They make the patient a danger to those in contact with him. Isolating of patients and the wearing of a mask covering mouth and nose when one approaches them are necessary Scrupulous handling of discharges from pustules and ulcers and ruptured buboes is self-evident.

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SCLEROMA RESPIRATORIUM (RHINOSCLEROMA)

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DEFINITION

Rhinoscleroma is an infectious disease of the respiratory tract with formation of granulomatous tissue of characteristic pathological structure, occurring from the nose to the bronchi and very probably caused by infection with *Klebsiella rhinoscleromatis* (VON FRISCH).

HISTORY

Rhinoscleroma was first described in 1870 by HEBRA (Vienna) as a disease of the nose. VON FRISCH (1882) isolated capsulated bacilli from the lesions. Afterwards other diseases known as laryngitis subglottica, chorditis vocalis hypertropica etc., were recognised as other localisations of the same process.

EPIDEMIOLOGY

Rhinoscleroma is endemic in many countries. One of the principal foci of the disease is Eastern Europe (the Ukraine, White Russia, Poland and Galicia with spreading in the adjacent countries). In Southern Switzerland and Northern Italy a second focus exists, possibly imported from Eastern Europe In the United States of America many cases have been observed, probable mostly imported, but perhaps autochthonous cases also occur In South America the disease occurs in Brazil Chile Argentine and Peru. Central America is

another major focus (San Salvador Guatemala, Costa Rica, Colombia, Cuba) as well as Mexico and Martinique.

In Africa a major focus occurs in Egypt In Morocco Algeria and Tunis a few cases have been observed Perhaps the disease also occurs in Central Africa.

In Asia, India and Indonesia are major foci some cases have occurred in Siberia, China, Iraq and Hawaii

Altogether about 3000–4000 patients are known over the whole world without any doubt more exist. The disease is by no means rare it is of sufficient importance to justify more extensive examination of the population of many of the countries mentioned

The distribution of scleroma respiratorium in circumscribed foci suggests that it is a contagious disease It attacks the poorer population. Bad housing insufficient food and very primitive living conditions (sleeping closely together in badly ventilated houses may be of great importance) are present in all major foci. It is essentially a disease of the great unwashed These circumstances will cause repeated infestation over a long period, which seems necessary for the development of the disease In this (and other) aspects the epidemiology of scleroma closely resembles that of leprosy Infection appears to occur directly from man to man it may take place by inhalation of droplets from a coughing or sneezing patient, or possibly by direct contact.

The contagiousness is clear from the observation that occurrence of multiple cases in one family is quite common. KOUWENAAR and others found in Sumatra (Indonesia) among 102 housemates of 27 patients with scleroma, 8 new cases, 7 carriers of *Klebsiella* and 5 persons with a positive complement fixation test so the patients had infected 20 % of the inmates of their abodes SIVAK reported a 30 infection in a family in Slovakia.

It appears that rhinoscleroma is an old disease, which is slowly disappearing with the advent of better hygienic conditions

AETIOLOGY

Klebsiella rhinoscleromatis a Gram-negative capsulated bacterium is found in the pathological tissue of patients suffering from this disease. It can be cultivated easily from almost all patients, but it is necessary

to take material from the deeper layers where the inflammation is still active. In pathological slides the bacterium can be seen in the cells of MIKULICZ, which cells are characteristic of this disease. *Kl. rhin.* is also found in a small number of healthy people living in close contact with the patients apparently these people must be considered as healthy carriers. Outside the foci of scleroma the bacterium has never been found.

Some authors believe that the causative agent is a virus and Klebsiella only a symbiont. The peculiar *geographical distribution* of rhinoscleroma, (see epidemiology) speaks against this hypothesis.

SEROLOGICAL TESTS

Extensively used in diagnosis and epidemiological examination (field work) is the complement fixation reaction, performed with an extract



495 Hebra nose in rhinoscleroma.

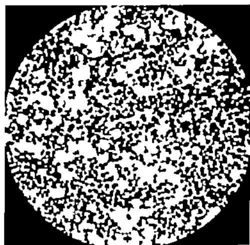
of the Klebsiella as antigen. NEUBER and ADAMS found a positive reaction in 80–90 of the manifest cases, WOLFF in 92½ %. With good technique non-specific reactions occur very seldom (WOLFF 1 %) perhaps ozaena may give a positive result. According to ALOOKER a negative reaction in a suspected patient may be converted into a

positive one by intravenous injection of tartar emetic. Again, in persons living in contact with patients positive reactions may be found.

The agglutination reaction with Klebsiella gives inconstant results. An allergic skin test by intracutaneous injection of killed Klebsiellae gives better results but the observation must be prolonged for at least 8 days as a reaction in the first 3 days is aspecific.

PATHOLOGY

The scleromatous process consists principally of a dense infiltration with plasma cells with some lymphocytes and leukocytes. Between



496 Plasmocytic infiltration and a multitude of Mikulicz cells.

these plasmocytes round red bodies are found, sometimes in a cell with a still recognisable nucleus sometimes isolated the bodies of RUSSELL or PELLIZARI. These are probably plasmocytes with hyaline degeneration. They are not specific, as they are found in many plasmocytic infiltrations. Specific are the MIKULICZ cells large cells with a frothy aspect usually only consisting of a pycnotic nucleus, small strands of protoplasm and a membrane, so that at first sight these cells give the impression of empty holes in the infiltration. In young granulomas many bloodvessels are found in older infiltrations

connective tissue has developed often with hyaline masses spread through the plasmocytic infiltration.

SYMPTOMATOLOGY

The granulomatous process may occur in the greater part of the respiratory tract, from the nose and mouth to the larger bronchi. They develop simultaneously or successively in different places as separate affections, and in each place the infiltration may invade adjacent organs.



497 Rhinoscleroma infiltration of the nostrils and upper part of the lip.

In many cases the process starts in the nasal cavity often the floor or the septum, soon attacking the skin, especially the tip and wings of the nose and the upper part of the lip under the nostrils (Fig 497). Later on the nose becomes very large, by progression of the infiltration under the skin, which becomes bluish red, and by filling the whole nasal cavity with granulomatous masses (HEBRA's nose, Fig 495) At first the granulomas are soft and bleed very easily later on, with the development of connective tissue they have the consistency of wood or cartilage. They are often very painful to touch. The skin remains

unbroken for a long time The lesions are sharply circumscribed, and the surrounding tissue does not display any reaction. Perhaps an atrophic stage (the pseudo-ozaenic form of scleroma) precedes the development of granulomas (PUTSCHKOWSKI)

From this first localisation the scleromatous process may spread along different paths into the para nasal sinuses, the upper lip (Fig 495) (with formation of granulomas in the mucosa) the palate (sometimes



498 Arrest d tage following ulceration and destruction of the nose.

with perforation into the nose) the pharynx (arcus pharyngis, uvula, choanae fornix pharyngis) the Eustachian tubes (with tinnitus and deafness owing to occlusion of the tube) or the lacrimal duct (sometimes with development of a fistula)

Another primary localisation is scleroma of the larynx, beginning under the glottis and later attacking the vocal chords, so that the voice becomes hoarse or aphonic. Stenosis may develop and suffo-

cation is a real danger Other sequelae are retraction of the epiglottis and development of oedema or laryngeal perichondritis

Granulomas may also develop in the trachea and the larger bronchi. The cervical lymphatic glands are enlarged in most cases.

The patients do not suffer unduly from the disease, unless laryngeal stenosis develops, and for a long time disturbances in general health are only slight. The granulomata may grow for many years, usually rather slowly In the course of years however many cases show a decrease in size of the granulomata, usually by retraction of the newly developing connective tissue, sometimes by ulceration and massive destruction of the tumour followed by cicatrisation. In this way a quiescent stage is reached with large internal and external defects, but with temporary cessation of growth of the lesions. In one single patient different stages of growth and destruction may be present at the same time. (Fig 498)

These destructions and especially the retractions give way to new complications. In the nose a very narrow circular stenosis may be found, as a diaphragm or funnel. The external nose may disappear. Cicatrisation in the pharynx, larynx and trachea, often with development of synechiae between the different parts may produce stenosis, difficulties in swallowing, dyspnoea etc.

The chief localisations of the disease vary in different countries sometimes scleroma of the nose dominates, sometimes the larynx is attacked most frequently *e.g* in Indonesia scleroma of the larynx is only very seldom seen.

Scleroma is a disease of the young adult 70–80 % of the patients develop their first symptoms between the ages of 20 and 35 years. Men are more frequently attacked than women.

DIAGNOSIS

The diagnosis is based on the clinical picture, bacteriological exami nation serological tests especially the complement fixation reaction, and the pathological picture. The clinical picture is very characteristic, and in most cases the initiated can easily differentiate scleroma from tumour lupus, lues, framboesia or leprosy The residual form with cicatrisation of the external nose may closely resemble lupus or rhinopharyngitis mutilans (gangosa, yaws) In true gangosa, however

the Wassermann reaction is nearly always positive. The initial and atypical forms as e g the atrophic form, are difficult to evaluate, and here the other diagnostic methods are of greater importance.

THERAPY

X ray therapy repeatedly applied for a long time to prevent relapses, has been reported to give satisfactory results A danger is the formation of cicatricial tissue in the larynx with stenosis and danger of suffocation.

Treatment with polyvalent vaccine made from Klebsiella rhinoscleromatis has been developed by NEUBER and very good results have been reported It is advisable to alternate these injections with injections of gold preparations, combined with transfusions of blood or serum from convalescent patients (NEUBER, BELINOFF)

Some experiments have been made with the prolonged use of streptomycin, apparently with satisfactory results (DEVINE)

In cases in which the growth of the granulomata, secondary cicatrisation or even acute glottic oedema endanger life by suffocation, surgical intervention is indicated Plastic operations may be helpful. The stenosing processes in the nose or the malformation of the pharynx can also be dealt with surgically Large external tumours can be ablated

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GRANULOMA VENEREUM (DONOVANOSIS)

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DEFINITION

Venereal granuloma is a chronic infectious disease, which is caused by the *calymmato-bacterium granulomatis* (also called *donovania* or klebsiella granulomatis) and which is characterized

(a) clinically by an extensive ulcerating and granulomatous and scarring process of the skin and subcutaneous tissue, particularly of the pudenda but also of extra-genital location.

(b) histologically by the presence of Donovan bodies with large mononuclear cells. The condition is auto-inoculable and only slightly transmissible It is not known if the term "venereal" is appropriate because in many cases infection is probably not conveyed by sexual contact.

Synonyms are *ulcerating granuloma of the pudenda serpiginous ulcer of the genitals tropical granuloma sclerotic granuloma of the pudenda, genito-inguinal granuloma groin ulceration chronic venereal ulcer contagious granuloma* and most confusing *granuloma inguinale* because this term is often confused with lymphopathia venerea.

EPIDEMIOLOGY

The disease is widespread in many tropical areas It is also seen in temperate regions (imported by sailors) of the old and new world, particularly in the coloured race. Some authors state that it is also more frequently seen among women than among men, although

others affirm the contrary In Brazil there is a predominance in the female.

HISTORY

The disease, first described by MacLeod in India (1882) under the name of "serpiginous ulceration of the genitals" received more attention owing to the publication of Daniels and Conyers from British Guiana in 1896 In 1905 Donovan discovered the causative organisms which he called *calymmatobacterium granulomatis* Flu in Surinam as well as Vianna and Aragão in Brazil drew attention to its resemblance to Friedländer s *bacillus mucosus capsulatus* which is easily cultivated on various common media and which is pathogenic for animals in contrast to Donovan's bacillus. In 1882 Frisch described a similar organism in rhinoscleroma which is also easy to cultivate. In 1912 Aragão and Vianna rebaptized the calymmatobacterium granulomatis by giving it the name of *Klebsiella granulomatis* In 1943 Dienst and Greenblatt classified the organism with the protozoa.

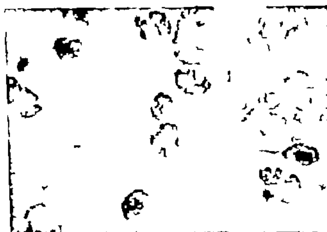
AETIOLOGY

Granuloma venereum is caused by the 'Gram-negative Donovan s *calymmatobacterium granulomatis* also called *Klebsiella granulomatis* be cause it should not be regarded as a bacillus (Dienst and Greenblatt) but a kind of protozoön. It may be found together with streptococci (Mflenet) When spirochaetes or spirilla are found, one should consider mixed infection with syphilis or tropical ulcer

The fact that many cases of venereal granuloma cannot be attributed to venereal infection has thrown doubt on the theory of the disease being a venereal disease, as is the fact in syphilis and gonorrhoea. It is even not excluded that an insect may prove to be the transmitting agent Nevertheless most cases occur in the adult, only a few cases having been reported in children or among the aged.

Parturier and Bierman state that venereal granuloma is in fact a disease of the skin and corium which does not attack the lymphatics. The genital predilection of the disease caused Greenblatt and his co-workers to suggest that the Donovan bodies spread from a primary focus *via* the lymphatics to the pudenda. In two cases biopsy of lymph nodes from underneath extensive venereal granuloma substantiated

this theory *Animal inoculation* has been affirmed by some authors but denied by others, principally by the Georgia University group.



499 Calymmato bacteria in three mononuclear cells.

Some workers believe that they have managed to cultivate the causal agent of the disease while others have failed to do so ANDERSON reported the cultivation, in the yolk sac of living chick embryos, of a micro-organism which has all the morphological characteristics of



500 Granuloma venereum: vegetative form. (*Willcox, London*)

the DONOVAN organism but which so far has not been cultivated on ordinary culture media and is not pathogenic to mice, dogs or



501 Granuloma venereum serpigino-vegetative form



502 Granuloma venereum ulcero-vegetative form.

monkeys The germ is auto-inoculable and some authors believe it to be strictly a parasite of human tissue

It can be stained by WRIGHT's or GIEMSA's method, by DELAFIELD's hematoxylin with eosin and by silver impregnation. It is Gram-negative. In the acute process or in the early stages of its development the germ is not encapsulated. The nucleus of encapsulated forms resembles a small curved bacillus and shows one or two terminal swellings simulating polar bodies; it may appear diplococcoid. *Atypical forms* with a diphtheroid structure, or appearing as non-encapsulated or diplococcoid forms surrounded by a zone of rarefaction, are often found. The different interpretations given as to the nature of the body are due to its polymorphism. In sections the affinity of the intracytic



503. Bilateral granuloma venereum, vegetative form.
N. B. Leukoderma of the glans penis, probably a form of albinism.

bodies for silver salts is characteristic; these bodies stain black to brown with a closed safety pin appearance because of their elongated ovoid intensified polar staining reaction. MOTARA and DIENST proposed a new staining procedure which demonstrates additional characteristics of the DONOVAN body and further differentiates it from the other bacteria of the Klebsiella group, e.g. FRIEDLÄNDER's bacillus and the Klebsiella rhinoscleromatis, which are readily cultivated and are pathogenic for laboratory animals, this being not the fact with DONOVAN's bacillus (JOHNS). The search for the organism should be prolonged and careful for at times it is difficult to find.

Before taking material for smear preparations, the lesions should be

bathed with physiological solution. The material should be collected rapidly by means of scraping or curetting the edges of the lesions which are the seat of greatest activity of the pathological process The search for the germ in material collected at these points is more efficient. The germs are more abundant in frankly vegetative cases and rare in slowly evolving or receding ones The presence of associated germs such as fusiform bacilli and spirilla may confuse the diagnosis. The causal agent may occur intra and extra-cellularly standing out clearly against the light pink background of the preparation. Still diagnosis should preferably be based on the presence of intra-cellular bodies

SYMPTOMATOLOGY

As *the initial stage* of the disease causes so little inconvenience to the patient, it is often overlooked or not given attention, for which reason



504 Granuloma venereum on the penis. Ulcerative type. *(Fatal—San Francisco)*

the incubation period has not accurately been established It is however said to vary between two days and three months

The location is most frequently on the pudenda, the genitals, perineum in the groins and sometimes even in the anus, rectum and colon the uterus fallopian tubes, ovaries, bladder etc. The condition

may also be present in the face (particularly the nose (*vide* the chapter on rhinoscleroma) and lips), the pharynx and larynx, the neck, the back of the hands, the legs where it may even extend to the bones[1]

"*Metastases*" (third stage of the disease) may occur in the liver spleen and bones THIERFELDER has described *a fourth stage* revealing paresis of the legs and the rectum. The patient may die from paralysis of the diaphragm.

The disease commences as a papule or nodule and gradually one of



505 Granuloma venereum progressive ulceration.
(Fazal San Francisco)

the many forms develop These forms can be classified as follows making a little deviation from HALTY's classification

(A) *Ulcerative forms* ulcero-vegetative, serpigino-ulcerative, ulcerative and terebrant.
(B) *Papillomatous and vegetative forms* elephantiasic, nodular papulo-hypertrophic or chancriform, serpigino-vegetative, condylomatous, scrofulo fungous and cicatricial.
(C) *Mucous forms*
(D) *Mixed forms*

[1] Oral and other extra-genital involvement has been reported in 3 to 6 % of the cases (RAJAM [illegible] and [illegible] THOMAS, PALIK and SCHNEIDER)
(Ref Br 14)

The ulcero-vegetative form also termed HALTY's type, is most frequently met with. It is located in the pudenda. This condition may begin as a sharply defined ulcer with an irregular reddish granulated base Sometimes it is covered by detritus. The base is firm, the ulcer being still not adherent to the underlying tissue, thus retaining mobility The ulcer is not painful, it may bleed easily it may scar partially and it produces a fetid odour There is no adenitis in those cases which are not secondarily infected.

The serpiginous-ulcerative form has a migratory character and grows in



506 Granuloma venereum of the nose (rhinoscleroma and granuloma venereum are both caused by klebsiella).

the folds of the groins and the genitals, leaving behind zones of scarring tissue In *the ulcerative form* the scarring feature is slight in comparison with the progressive ulceration

The terebrant form is most common in the female It shows oedema and the ulceration is deep from the beginning This form may extend over a large area and may penetrate into the internal genitals and anus thus becoming difficult to distinguish from esthiomène in lymphopathia venerea.

The papillomatous or vegetative form may reveal elephantiasic growth and particularly affects the labia majora and minora, and the clitoris.

This type is frequently seen in the Argentine (HALTY) and may be complicated by ulcers and fissures no lymphangiectasiae are seen, as is common in elephantiasis due to filariasis

The nodular type shows soft nodules which sometimes disappear spontaneously This form has been termed "*pseudobubo*" by GREENBLATT and others

The papulo-hypertrophic or chancriform venereal granuloma also called STAJANO's *type* sometimes represents the initial lesion, although it is also seen as a satellite form of the others. In the former it may be solitary and be located in the coronary sulcus or in the corner of the vulva, in the latter a multitude of chancres" may be seen. The base is firm and swollen.

The serpiginous-vegetative form affects the natural folds, genitals and perineum and has a cerebriform or fungoid appearance.

The condylomatous form consists of sessile, pediculated and acuminate papillomata, which may become confluent, thus forming plaques with a quite sharply defined outline.

The scrofulo-fungous type has been described by Brazilian authors as swellings which become soft and fistulated From the depths of the fistulae exuberant polypoid dark purple tissue, which easily bleeds, may protrude This form originates in regions with a firm dermohypodermic infiltration.

The cicatricial type results from a special reaction of the patient to the infecting agent, which produces keloids. It is chiefly found in the coloured race, which has a disposal to keloid formation. In the keloid tissue DONOVAN bodies may be found. In old cases COLE noted lymphatic obstruction, leading to a kind of Hottentot apron of the clitoris.

The mucous forms are initially congestive and infiltrated, with an irregular surface and a "granite" aspect. When fully developed they may assume the aspect of one of the cutaneous forms In the female however there may often be ulceration and bleeding

The mixed form is a mixture of some of the above mentioned types

General signs are not definitely known. Fever may be due to secondary infection, malaria, etc.

LABORATORY DIAGNOSIS

A complement fixation test antigen from excised tissue intracutaneously injected and a scratch test have already been used for the diagnosis of venereal granuloma but the specificity of any serological allergic or other immunity reaction so far proposed has been denied.

Hyperglobulinaemia, anaemia or *leucocytosis* is met with but these are not peculiar to the morbid process

Animal inoculation is not suitable for establishing the diagnosis. Diagnosis is based on the finding of DONOVAN bodies in smear Several examinations should be carried out and many slides prepared, for the smear is often contaminated with other micro-organisms and because of the fact that only a small number of DONOVAN bodies may be present

TORPIN GREENBLATT and PUND recommend the following routine examinations

1 WASSERMANN's and KAHN's tests
2. Search for DONOVAN corpuscles gonococcus, fusiform spirilla, DUCREY's bacillus and fungi
3 TETSUDA REENSTIERNA s test
4 FREI s test.
5 Biopsy of a piece of tissue which should be divided into 2 parts one for histological examination and one for a smear preparation.
6 Culture of closed lesions

PATHOLOGY

Some authors believe that in venereal granuloma there exists a characteristic histological picture, while others do not share this belief

We agree with the latter for the histopathological alterations which take place are those of an exudative purulent inflammatory process associated with productive modifications constituting a veritable pseudo-epitheliomatous hyperplasia.

The entire cutis and subcutaneous tissue are densely infiltrated with plasmocytes lymphocytes and a smaller number of fibroblasts. There are also seen clear cells with faintly-stained nucleus and foamy protoplasm full of parasites

The parasite containing cells are histiocytes which present no

pathognomonic features except the presence of DONOVAN corpuscles.

PUND and GREENBLATT believe that there exist "pathognomonic mononuclear" cells (endothelial cells?) (VON HAAM)

In the chronic hypertrophic lesions there is a massive development of collagenous tissue surrounding nests of plasma cells and lymphocytes

DIAGNOSIS

This is of great importance because this disease may in certain cases, present features which are hardly distinguishable from other venereal or non venereal genital affections.

Ducrey's chancre especially in its condylomatous phagedaenic and



507 Serpiginous chancroid simulating granuloma venereum.
(van Dyke and Oudendal I Kayser "Verdrachten Trop. Huidziekten")

serpiginous forms, and to a lesser extent adenitis due to soft chancre, must be differentiated from venereal granuloma.

Problems in differential diagnosis are also presented by the following diseases *genito-ano-rectal syndrome of Nicolas Favre's disease* especially in cases of association, *syphilitic chancre ulcero-serpiginous syphilides syphilitic condylomas venereal warts* (condylomata acuminata) *carcinoma of the external* and even of the *internal genital organs genital leishmaniasis yaws fungoid granuloma pyoderma bromoderma* and *iododerma blastomycosis* and other mycoses

The complexes "*in loco*" (GOUGEROT) should not be forgotten nor the morbid associations from a general point of view all the laboratory

and clinical data, which can facilitate the classification of the case, should be employed It should be noted that tropical granulomas are eminently polymorphous and that their lesions imitate one another on this account even skilled observers find themselves constantly face to face with problems which, for their satisfactory solution, require careful observation and series of routine examinations referred to above.

EVOLUTION, COMPLICATIONS AND PROGNOSIS

The course of venereal granuloma, whatever its clinical form may be, consists of a phase of expansion interrupted by short phases of spontaneous though incomplete cicatrisation and finally a period of cure.

The granuloma does not spare its scars and so the ulcero-papillomatous process may reappear in frankly cicatrical tissue.

Another point worthy of note is that the abundant secretion never forms scabs over the lesions but merely a pultaceous covering layer

Before the use of tartar emetic and antibiotics as therapeutic measures the evolution of the disease was long and slow and the patient could remain strong and apparently healthy for many years. But at last he would begin to pine away his physical forces would abate till he finally fell into a state of cachexia unless meanwhile he succumbed to some intercurrent disease.

With venereal granuloma other diseases may be associated such as gonorrhoea fuso-spirochaetosis syphilis DUCREY's chancre NICOLAS-FAVRE, and occasionally malignancy may be superimposed.

As to NICOLAS-FAVRE's disease or lymphopathia venerea, particularly its late stage of esthiomène may cause confusion.

Besides recto-vaginal fistulae with, possibly cicatricial stenosis at the level of the urethra and anus, there is deformity of the labia with elastic oedema lymphangiectasis and ulceration which frequently assumes a terebrant aspect in both conditions a positive FREI's reaction and iliac adenitis indicate lymphopathia venerea.

The prognosis of venereal granuloma has been entirely modified by the use of antibiotics such as streptomycin chloromycetin, aureomycin Since the introduction of these drugs the prognosis has become favourable When tartar emetic is used there is often an *emetic resistance*

THERAPY

Before the introduction of antibiotics treatment was effected with *tartar emetic anthiomalin* and *fuadin radio-therapy* and the *electric scalpel* *The tartar emetic treatment* was discovered by GASPAR VIANA both for American cutaneous leishmaniasis and for venereal granuloma. A 1 % solution of tartar emetic in physiological saline was injected intra venously in doses of 2, 3 4 and 7 ml at intervals of 3 to 5 days until the dosage of 10 ml was reached in a series of 20 injections

Radiotherapy has also been tried in doses of 150 KV 4 mA, F.S.D



508. Pseudo granuloma venereum due to blastomycosis.

30 cm, 3 to 4 mm Al filter up to a total of 450 to 600 r The intervals were from 21 to 40 days.

In emetic resistant cases the electric scalpel was also used.

Nowadays, however, treatment with *streptomycin* has supplanted all the other methods and has opened new vistas in the realms of venereal granuloma therapy

BARTON and his colleagues GREENBLATT KUPPERMANN and DIENST have used this form of treatment with great efficacy The daily doses ranged from 0.3 to 1 g administered in 6 equal doses per 24 hours at 4 hour intervals. Total doses varied from 3.3 to 4 6 g given over a period of time extending from 6 to 46 days. Streptomycin may produce

toxic reactions such as fever maculo-papular rash, fine vesicular eruption or oedema Chloromycetin is also efficacious but thyrothricin and penicillin have not proved effective.

PROPHYLAXIS

This is based on the extinction by modern means of treatment of the sources of contagion on the abstention from intimate contact with those affected by the disease, on teaching the masses the facts about body hygiene, promiscuity and the treatment of cutaneous abrasions.

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CHAPTER 24

PYODERMA

A. GIRDWOOD FERGUSSON – Glasgow
C. A. EINDHOVEN – Surabaya

By pyoderma is understood a skin disease provoked by pyogenic organisms. This is directly true in many instances but various dermatoses which are not primarily caused by such organisms may become secondarily infected therewith, usually on account of scratching (*e g* secondarily infected scabies).

Purulent dermatoses which are not caused by pyococci are not usually ranked among the pyodermas. Numerous diseases of this nature readily come to mind, varying from virus states such as orf and eczema vaccinatum to cutaneous diphtheria, amoebiasis cutis and glanders. Again a pyococcal disease such as erysipelas is included in the group despite absence of frank pus formation.

The conditions to be considered below have in all probability been most clearly defined by DARIER as follows —"*pyoderma is a dermatosis caused by pyococci and* generally *purulent*"

CLASSIFICATION

Pyoderma is generally conceived to exist in two principal forms, depending upon the infecting organism, but, since mixed infection is frequent, this subdivision is not by any means reliable. Only where fresh lesions contain predominantly either streptococci or staphylococci can we speak with certainty of streptoderma or staphyloderma.

It is interesting to note that staphylococci appear to have a predilection for hair follicles and sweat ducts. They are in fact mainly

responsible for the production of folliculitis, furunculosis and abscesses of the sweat glands. Streptococci, on the other hand, more often provoke superficial, non-follicular pyoderma.

The principal diseases of the group under consideration are erysipelas impetigo contagiosa, ecthyma, superficial and deep follicular infections (impetigo staphylogenes sycosis, furunculosis and carbunculosis) hydrosadenitis infectious eczematoid dermatitis and pemphigus contagiosus Also included are one type of intertrigo dermatitis repens, pustular bacteride (ANDREWS) granuloma pyogenicum and the deeply ulcerative conditions usually grouped under the general title of pyoderma gangraenosum.

AETIOLOGY AND PATHOGENESIS

It is known that pyococci may occur as saprophytes on the surface of the skin. When, therefore, such organisms are found in the fluid of vesicles, bullae and pustules in certain dermatoses, this is not conclusive proof that the diseases have been caused by them. Although the common pyodermas (*e g* impetigo and ecthyma) have in the past been considered to be exclusively streptococcal states, modern views on the matter show a considerable divergence of opinion. HIEMCKE and RUYS were able to demonstrate streptococci in only 10 per cent. of cases of impetigo CRUICKSHANK found haemolytic streptococci in over 50 per cent. of cases. EPSTEIN on the other hand, found streptococci in only 2 per cent. of his series as against staphylococci in 50 per cent. and both organisms in the remainder There is little doubt, however that impetigo may be caused by either streptococci or staphylococci and that the trained observer is often able to distinguish clinical differences in an otherwise very specific skin picture which point to one or other bacterium as the basic aetiological factor (DAVIES *et al* 1945 BIGGER and HODGSON 1943 SHEEHAN and FERGUSSON 1943) The difficulty experienced by BIGGER and HODGSON and to a lesser extent by SHEEHAN and his co-worker in fulfilling KOCH'S postulates by reproducing the disease by inoculum of lesion fluid or cultured organism however points to factors other than simple infection as regards the aetiology of the pyodermas. Such factors remain as yet hypothetical and offer a fruitful field for further study

The streptococci of importance in the production of pyoderma are

those of haemolytic nature. Such organisms are apparently causal of erysipelas and the crusted type of impetigo.

Staphylococci occur more often than streptococci as apparent saprophytes on healthy skin. Organisms such as *S albus* and *citreus* are rife and modern laboratory tests tend to show that many of these achromic variants of *S aureus* are no less pathogenic than the latter itself. It would appear, therefore, that the term *S albus* as applied to a non pathogenic or weakly pathogenic skin commensal has now become largely meaningless (HARRIS, 1948) *S aureus* a pathogen, is also commonly found on a healthy skin surface, but it is probable that a potent nidus of this organism and of haemolytic streptococci exists in the nasal mucosa of most individuals.

Staphylococcus pyogenes aureus is the basic factor in the production of purulent disease of the hair follicles and sweat glands, pemphigus contagiosus, impetigo bullosa neonatorum, infectious eczematoid dermatitis and granuloma pyogenicum. It is probable also that this organism (and some of its achromic variants) is largely concerned in the production of dermatitis repens, pustular bacteride and gangrenous pyoderma in all its many forms.

It is therefore, obvious that staphylococci are the most important of the pus-forming organisms as regards disease production in the skin preventive and therapeutic measures in this field have, therefore, to be based upon a clear recognition of this fact. Further the importance of general debility as an aetiological factor in the case of staphylococcal pyoderma must never be underestimated. Debilitating systemic diseases such as diabetes, chronic nephritis, ulcerative colitis carcinomatosis and in the tropics protozoal and other infections have to be kept in mind in any approach to the problem of rational therapy

ERYSIPELAS

Erysipelas is a disease of streptococcal origin characterized by the acute appearance of a sharply delimited, reddish brown erythema, lightly thickened by oedema, as can be seen and felt especially at the edges. The patient is feverish and the regional lymphatics are swollen. Bullae appear in rare cases. Erysipelas often appears around or in the vicinity of wounds, and is commonly seen on the face. It usually disappears spontaneously within a fortnight, but there are frequent

relapses, and the disease may end fatally in children and the aged.

What is called *recurrent cellulitis* (or elephantiasis nostras) is a form of relapsing erysipelas leading to elephantiasis of the affected part, *e g* a leg or an arm, lip ear etc.

By the term *erysipeloid* (ROSENBACH) is meant an affection resembling erysipelas It is not febrile and occurs chiefly on the hands of persons who in preparing raw meat or raw fish, have become infected with Bacillus erysipelatis suis or erysipelothrix rhusiopathiae (see also erysipeloid, under pellagra) By *erysipele de la tete* or *mal de morada* is understood cutaneous onchocerciasis a filarial disease.

IMPETIGO

Impetigo is one of the most important pus-coccal diseases. Although the term impetigo" forms part of the nomenclature of various dermatoses, in dermatological parlance the term refers to *impetigo vulgaris* or *contagiosa* (TILBURY FOX) in which crusts are formed *from the start* (ab impetu ") A tropical disease is *impetigo bullosa* in which crusts are not formed ab impetu and in which they do not dominate the syndrome. This is dealt with below

In those cases where impetigo occurs secondarily to another skin disease, we say that the latter disease has been *impetiginized*. In regard to this concept two things should be kept in mind, *viz*

(a) a clear distinction must be made between a crusted and an impetiginized eczema. In the former we have to do with serous or medicamentous crusts associated with a moist eczema In the latter with purulent crusts of impetigo superimposed upon an eczema

(b) It is also important to distinguish between "*eczéma impétiginisé*" in which the eczema has been impetiginized, and *eczéma impétigineux* when the eczema is caused by pyococci. The latter disease is more or less synonymous with infectious eczematoid dermatitis.

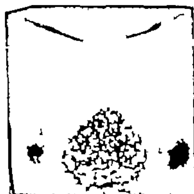
IMPETIGO VULGARIS OR CONTAGIOSA (TILBURY FOX)

In this form of impetigo which is the most frequently encountered, thick yellow or grey crusts appear They are chiefly found on the face on the hair-covered part of the head (often on account of scratching due to pediculi) and to a lesser extent on the trunk, arms and legs.

The surrounding skin shows hardly any change. In those cases where a large part of the face is covered with crusts the condition is known



509 Streptococcal impetigo vulgaris, there are no blisters but thick crusts are present. *(Siemens–Leyden)*



510 Streptococcal impetigo on the breast. This began with crust of the size of a nailhead which grew to this size within a fortnight. *(Simons – Amsterdam)*

as *impetigo larvalis* Sometimes the regional lymphatics are swollen, leading to lymphangitis

Impetigo vulgaris, which is often found as a complication of sca

bites, burns or pediculosis capitis is ranked with the streptogenic pyodermas.

As sub-types are classed, *panaris sans-épidermique* or *bulla rodens* of the hand, *stomatitis angularis* or *perlèche* (see, however the chapter on



511 Impetiginized yaws.

(Alers-Carrapo)

pellagra) and furfuraceous impetigo (pityriasis alba vel streptogenes). A special form (without crusts) is intertrigo of streptococcal origin.

Impetigo vulgaris must be differentiated from diphtheria cutis and tropical yaws, both of which, however may also be complicated by impetigo.

IMPETIGO STAPHYLOGENES BULLOSA

Although staphylococci may set up an impetiginous eruption resembling impetigo vulgaris, they also appear able to provoke a distinctive form of the disease. This form is characterized by the appearance of large blisters which soon burst—sometimes while still in statu nascendi—and by the subsequent formation of very thin, light yellow crusts resembling pieces of dried-up discoloured collodion. These



512 Blisters and purulent crusts of Impetigo bullosa or pyosis MANSONI. *(Siemens–Leyden)*

blisters too appear on the face (not so much on the hair-covered part of the head) but frequently also on the rest of the body. The affection spreads rapidly by auto-inocculation in babies this leads to *pemphigus epidemicus neonatorum* (impetigo bullosa neonatorum) which, again, may pass into *dermatitis exfoliativa infantum* (RITTERSHAIN OF RITTER's disease). The disease is not so common as impetigo vulgaris in temperate zones. It is described in further detail in the next chapter since, though rare in Europe, it is extremely frequent in the tropics where it is known as pemphigus contagiosus. In Europe this condition is

occasionally found among farm labourers (in the groins and armpits) and as a complication of scabies.

IMPETIGO STAPHYLOGENES FOLLICULARIS (BOCKHART) OR SYCOSIS SIMPLEX

This pyoderma is characterized by the appearance of multiple, very small follicular pustules through which, here and there, a hair may be seen protruding. It is sometimes coupled with blepharitis of the same aetiology. Sycosis of the upper lip (moustache) is usually associated with or caused by rhinitis. Any hair bearing part of the skin may be affected.

BOCKHART's impetigo or *superficial folliculitis* which has a strong tendency to relapse, is *not*—in contrast to *deep folliculitis*—cicatricial. When scars are formed we have to do with deep folliculitis, furunculosis or folliculitis decalvans (which leaves a lasting multiple alopecia on the hairy parts of the head). See also *purulent folliculitis of the legs* (CASTELLANI, Vol. II).

While the term sycosis simplex refers to pyogenic folliculitis barbae *sycosis parasitaria* refers to deep trichophytic fungus infection in the region of the beard characterized by large painless granulomatous infiltrates in the affected skin. The conditions are frequently confused and must be carefully distinguished.

OTHER IMPETIGINOUS STATES

Some dermatoses bearing names to which there is some doubt as to whether they are entitled are impetigo rodens, impetigo miliaire and impetigo herpetiformis.

Impetigo rodens (DEVERGIE), better known as *acne necrotica* (BOECK) is a rare persistent and relapsing affection, which nearly always appears around the border of the hair and is characterized by small ulcers with a moth-eaten edge and a necrotic centre. The condition is probably of staphylococcal origin.

Impetigo miliaire (DARIER) is synonymous with tropical lichen (prickly heat) or miliaria rubra.

Impetigo herpetiformis is an acute bullous, sometimes pustular and urticarial dermatosis appearing in pregnant women especially on the trunk and sometimes also on the mucous membranes. It is a very rare affection whose origin is as yet unknown. A similar disease process is occasionally seen in males.

DEEP FOLLICULITIS, FURUNCULOSIS AND HIDRADENITIS

Apart from the non-cicatricial superficial folliculitis which has been described above there must be mentioned deep cicatricial folliculitis, which is also of staphylogenic origin. In Indonesia deep *folliculitis decalvans* of the hair-covered head is seen relatively often among Chinese who wear their hair short, and not often among the natives



513. "Collerette" of scales on hidradenitis, the latter being often wrongly called furuncles.

who wear the hair long and usually keep the head covered.

When deep folliculitis is a necrotic process it is called a furuncle or carbuncle. Such conditions are affections of the hair-follicles, in contradistinction to *hidradenitis* or sweat-gland abscess, which is often mistaken for furunculosis, particularly when involving body and limb flexures

ECTHYMA

Ecthyma is a form of ulcerative pyoderma appearing chiefly on the legs. It is characterized by irregularly shaped ulcers which are covered by purulent crusts from which pus oozes on pressure. Around the

crust there is an erythematous fringe The condition may be of either streptococcal or staphylococcal origin. It must be carefully distinguished from tropical ulcer due to VINCENT's symbiotic organisms.

PYODERMA VEGETANS

Pyodermites végétantes ("vegetating pyodermas) occupy a special place among the pyodermas. They are relatively rare and are very often not, at first sight, recognized as such indeed, some dermatologists do not class them with the pyodermas at all, *since many cases of this character*—and this applies particularly to *pyodermite végétante Hallopeau—are in*



514 Granuloma pyogenicum (erroneously termed botryomycoma) *(Siemens Leyden)*

fact examples of pemphigus vegetans Here there is little or no purulence crusts too are often absent. The affection does not respond to sulpha or penicillin therapy and often ends fatally after years of suffering

Pyodermite végétante is characterized by a proliferating dermal process which may assume different dimensions, sometimes appearing simultaneously in various parts of the body The diagnosis is difficult on account of the fact that pyococci may be found in many vegetating dermatoses and because it is often not possible to provoke the same morbid process with the cocci so found. The condition often follows *cutaneous injury* and is sometimes *typically noted* to arise on a pre-existing basis of chronic eczema or dermatitis. There is probably a

close analogy with acne conglobata, perifolliculitis abscedens et suffodiens (HOFFMAN), and with pyoderma gangraenosum (q v) granuloma pyogenicum is merely a very localised example of vegetating pyoderma.

Pyodermite végétante may resemble yaws or certain fungoid affections such as mossy foot (q.v), and must not be confused with malignant anthrax, bilharzioma or amoeboma. In the tropics "craw craw" is especially important in differential diagnosis (*cf* Vol. II) as also is granuloma inguinale.

ACRODERMATITIS CONTINUA (HALLOPEAU) OR DERMATITIS REPENS

This dermatosis is classed by some dermatologists among the pyodermas. The affection is probably caused by staphylococci It is characterized by a slowly spreading pustular dermatitis at one of the finger tips, in which the epidermis may be undermined. The condition may become widespread An allied disease process is the so-called pustular bacteride described by ANDREWS. Here there is an eruption composed of deeply seated pustules, usually first appearing on the mid-portions of the palms and soles and spreading outwards until the entire flexor aspects of the hands and feet are involved The disease process generally begins on one extremity and involves the others in a progressive manner Middle-aged adults are usually affected and there is no history of preceding injury

PYODERMA GANGRAENOSUM

This affection is not caused by staphylococci or streptococci alone, but also by Bacillus pyocyaneus. There may well be a synergistic action of these three organisms. Abscesses are formed, which break down and leave large ulcers. Allied conditions are dermatitis gangraenosa infantum, haemolytic streptococcal gangrene (MELENEY) and, as noted above pyoderma vegetans.

There must also be mentioned in this connection postoperative progressive bacterial synergistic gangrene. This condition has been described by MELENEY as wound infection of a peculiar type which usually follows drainage of peritoneal and lung abscesses or of chronic empyema. The wound region becomes carbunculoid and centrally

gangrenous with local colour changes varying from bright red in the periphery to purple around the gangrenous area, and is excruciatingly painful. There is a tendency common to all gangrenous pus-coccal processes, for the disease to involve the neighbouring healthy skin in a progressive fashion. Two organisms are generally incriminated, a micro-aerophilic non-haemolytic streptococcus in the spreading edge of the lesion and a staphylococcus in its central gangrenous portion.

Since this condition was first described, however many apparently



515 Meleney's ulcers.
(Prakken—Amsterdam)

spontaneous examples of similar character have been recorded. In these the process presented its characteristic features and bacteriology but appeared to arise de novo

THERAPY

The therapy of pyoderma is partly described in the next chapter It should especially be borne in mind that, in order to prevent relapses the skin should after recovery be given continued treatment with antiseptic applications and that the patient's clothing—particularly the underwear—should also be disinfected, the easiest way being to pass a hot iron over same This applies especially to those garments which cannot be dipped into a disinfectant solution or boiled, as well

as under circumstances where dry disinfection, *repeated a few times in succession* is impracticable. The patient should keep the nails carefully trimmed.

In impetigo internal treatment usually fails. Dieting vaccines, autovaccines, penicillin and internal sulpha-therapy are all inadequate. Only in those cases where a pyoderma is "deep" as in furunculosis and more particularly carbunculosis can any good result be expected from penicillin- or sulpha-treatment. It is true that injection of toxoids raises the antitoxin titer by more than twenty times but this nevertheless does not affect either impetigo or sycosis simplex (FORMAN). Local sulpha and penicillin-treatment may give good results but it is relatively expensive, and, moreover entails the risk of allergic eczema. Chloromycetin and aureomycin are still at the stage of clinical trial.

Simple treatment of impetigo entails softening crusts for one day by applying diachylon ointment, removing them with oil on the following day and treating the remaining erosive patches with boric acid or ½ per cent. sulphur calamine lotion. A good ointment to use after removal of the crusts is one consisting of ichthyol 1 oxydum zinci 3 vaseline ad 30 On account of the danger of lead poisoning one should be careful not to expose unduly large parts of the skin to diachylon for a long time. Another remedy which has been applied—with varying success—is gentian violet (½–5 per cent. aqueous or alcoholic solution) or "triple dye (*i.e.* crystal violet, brilliant green and trypaflavine). Erysipelas usually responds satisfactorily to local applications of ichthyol (10 %) in glycerin combined with parenteral penicillin.

In cases of prolonged folliculitis, epilation (usually temporary) is advisable. In any case it is wrong to allow the hair to grow Epilation may be carried out by roentgen irradiation. It should be pointed out to the patient that the hair does not fall out until about a month after irradiation, so that he will have to exercise patience. In cases of very obstinate sycosis, where irradiation is impossible, "plucking" the patient under narcosis may be considered for this purpose the beard must first be allowed to grow for about a week. The operation finished, the skin is treated for a few days with permanganate compresses (1 10 000), after which the patient is instructed to wash the affected parts with 1 1000 mercuric chloride in aqueous solution. If epilation is impracticable, it is still advisable *not* to forbid the patient to shave

This should be continued, with a good quality brushless shaving cream, the razor being disinfected each time. The shaving brush, impossible of sterilisation should be discarded until cure has been completed.

Cases of furunculosis often benefit greatly from exhibition of vitamin C in dosage of 300 mg daily combined with general ultraviolet light baths which have a generally bacteriostatic effect upon the organismal flora of the skin. As mentioned above, penicillin (parenteral) constitutes the optimum therapy of carbunculosis. Underlying and debilitating disease (e.g. diabetes mellitus) must be borne in mind when considering the management of staphylococcal pyoderma. Without specific treatment of such underlying states, measures directed towards alleviation of the skin disorders themselves will usually prove abortive.

It is useful to remember that overtreatment of pus-coccal disease of the skin often leads to failure. Skilful use of a few remedies should be the aim of the clinician.

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PYOSIS MANSONI
(Monkey Pox, or Impetigo Bullosa)

R. D G. PH SIMONS
Amsterdam

DEFINITION

Pyosis Mansoni—also called *impetigo bullosa tropica* or *pemphigus tropicus contagiosus* and, in Indonesia, "*monkey pox*"— is a pyoderma occurring mostly in the tropics, and caused mainly by staphylococci

It consists of smaller or larger bullae, with a turbid or purulent content, which may be surrounded by erythematous zones.

EPIDEMIOLOGY

Monkey pox—rare in Europe—occurs endemically in the tropics, and epidemically in separate groups, *e g.*, families. Paradoxically it is found there particularly among Europeans and much less often—nay hardly it at all—among the natives although the latter live far less hygienically and, for example bathe in the "kali" (river). As regards Europeans again, it is especially women and children (and particularly those newly arrived in the country) who are most often infected.

This is the prime characteristic of monkey pox.

AETIOLOGY

The second peculiarity about this disease, is that pyosis Mansoni is a staphyloderma which is not confined to the follicles as is usually the case but is caused by staphylococci which, for some unknown reason, behave on the skin like streptococci.

Both staphyloderma and streptoderma may be subdivided into superficial and deep inflammations of the skin.

The principal deep staphylodermata are furunculosis and hidradenitis (i.e. a deep sweat-gland abscess) both of which are cicatricial. In folliculitis decalvans—another deep pyoderma—bald patches on the head remain behind after recovery on account of scarring.[1]

The most important superficial staphylodermata are BOCKHART's impetigo, monkey pox and pemphigus neonatorum.



516. Pyosis Mansoni or impetigo bullosa

Different species of staphylo- and strepto-cocci may be present on the healthy skin. The reasons why they may suddenly set up a pyoderma, why staphylococci are strikingly organotropic and streptococci not, why, for instance, staphylogenic impetigo is highly infectious, while the cocci are relatively less virulent, whereas the furuncle

[1] This cicatrizing alopecia, which is seen especially frequently among Chinese, must not be confused with secondary syphilitic non-cicatricial alopecia.

is far less infectious while the "same" cocci are far more virulent—are all, as yet, unknown.

The micro-organisms provoking monkey pox are *Staphylococcus aureus* and—quite possibly also—*S. albus*. Inoculation tests with isolated species of staphylococci (MATZENAUER, KREIBICH, DOHI) caused bullae to appear after an *incubation period* of two days.

I. *Affected dermal organs: mostly staphyloderma*

1. Superficial
   a. Hair-sebaceous organs: Staphyloderma follicul. corporis, capitis et barbae (BOCKHART's impetigo), "miliaire pustule épilatoire".
   b. Sweat glands: LEWANDOWSKY's periporitis. (?) Prickly heat (?)
   Nails: Onyxis. Resembles other onychoses (*e.g.* mycoses), usually plus paronychium.

2. Deep
   a. Hair-sebaceous organs: furuncle and carbuncle, acne conglobata, folliculitis decalvans.
   b. Sweat glands: Hidradenitis (deep sweat-gland abscess in the armpit).

II. *Outside the dermal organs: both staphylo- and streptoderma*

A. *Staphyloderma*
   1. Superficial. Pyosis Mansoni, pemphigus neonatorum, staphyloderma bullosa manuum ("tourniole"), RITTER v. RITTERSHAIN's disease, impetigo bullosa faciei.
   2. Deep: Ecthyma staphylog. phlegmonosa, panaritiumosa. Botryomycoma[3]

B. *Streptoderma*
   1. Superficial. Impetigo vulgaris, streptogenic tourniole, perleche (angulus infectiosus) (sometimes secondarily infected with diphtheria bacilli)
   2. Deep: Erysipelas, Ecthyma. Phlegmona, sometimes paronychia.

From the above schematic list the correct nomenclature for pyosis Mansoni may be derived, namely *staphyloderma bullosa superficialis non follicularis disseminata endemica* (or, as the case may be, *epidemica*) *tropica*.

In dermatological practice the shorter, more convenient name "*pyosis Mansoni*" or "*pemphigus contagiosus*"[1] is used.

[1] In pemphigus contagiosus the bullae are smaller than in pemphigus vulgaris; the former [illegible] indeed, contagious, pemphigus vulgaris is not. The term "pemphigus" without an adjective refers to pemphigus vulgaris, which is a bullous dermatosis (not a pyoderma) ending nearly always fatally, and in no way related to monkey pox.

[2] The term "impetigo" is incorrect here. There is some difference of opinion regarding its actual signification, but if "impetigo" should be derived from "ab [illegible]

[3] Granuloma pyogenicum is to be distinguished from botryomycosis in animals (see chapter 1).

impetu"—*i.e.* "from the beginning"—then this would seem the most significant point about it.

For in impetigo crusts appear right at the outset. To the dermatologist who associates the presence with crusts in impetigo the name sounds strange when used with reference to monkey pox (a bullous condition). Moreover "impetigo bullosa staphylogenes faciei" is an altogether different staphyloderma frequently occurring on the face. The bullae are very large and burst very soon after their appearance. This impetigo is actually characterized by large yellow transparent crusts, with, maybe, an old bulla here and there.

SYMPTOMATOLOGY

In some cases the blisters may be the size of marbles, loosely pendulous ("bulles flasques") and partly filled with yellow liquid or pus. After a blister bursts there remains an erosion surrounded by scales, which persists for a day or two. This may either disappear or become covered by a purulent crust; it may also be pigmented, or, on the contrary, leukoderma may occur. There are no scars [1] and there are no general phenomena or irritation. If there is any itching, then this points to coincident miliariasis or ointment irritation.

Pyosis Mansoni may occur in a disseminated form. As the blisters readily burst, causing their infectious content to run over the healthy skin, is it obvious why monkey pox lesions are found especially in groups and in the large skin-folds. The disease, however, may spread rapidly over the body and be transmitted to other persons. The Japanese name "*tobichi*" which literally means "sparks flying across" as well as the name "monkey pox" indicates that the disease spreads rapidly. Each separate bulla exists only a few days—or hours, but owing to the auto-infection the disease may last a long time, unless proper treatment is instituted, in which case the duration of the disease need be hardly any longer than that of the separate bulla.

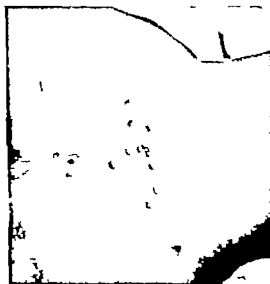
When a monkey pox bursts, an erosion becomes visible, surrounded by the remainder of the blister like a scaly collar ("collerette"). After this it changes into a pigmented—or sometimes, on the contrary, depigmented—patch, or disappears without leaving a trace.

Staphyloderma bullosa (or possibly pustulosa) superficialis may be subdivided as follows:

[1] Necrosis is sporadic ... in this case the disease has penetrated deeper into the skin, and causes scars reminding one of papulo-necrotic tuberculid.

Follicular forms	*Non-follicular forms*
1 Staphyloderma follic. bullosa superficialis	1 Impetigo bullosa faciei (crusts).
corporis	2 Staphyloderma superficialis bullosum manuum ("tourniole").
b barbae (sycosis simplex)	3 Pemphigoid neonatorum or Dermatitis exfoliativa VON RITTERSHAIN or RITTER disease.
c capitis (folliculitis et alopecia (non atrophicans) (an abortive form of bullae, or rather pustules. Not to be confused with the (deeper) folliculitis atrophicans, cicatricans and decalvans, with BROCQ's pseudopelade, or with alopecia postimpetiginosa streptogenes).	4 Staphyloderma bullosa superficialis non follic. disseminata (corporis) endemica tropica (monkey pox) = pyosis Mansoni.

A third peculiarity of monkey pox is that, when occurring in newly born babes, it (a) is known under another name (b) is then no longer



51 Pyosis Mansoni preference to the large folds.

confined to the tropics and (c) assumes a much graver character It is then called *pemphigus epidemicus neonatorum* The term "pemphigus" is

here again, misleading a fact of which I once saw clear evidence at a maternity clinic where pemphigus neonatorum had broken out I was given to understand that it was proposed to treat the babies with germanine since this was also used in cases of pemphigus vulgaris



518. Pemphigus contagiosus i.e. the malignant form of bullous staphylogenous impetigo.
(Simons Leyden)

This foolish notion has even been recommended in the literature by TILLING (*Derm med Wschr* 42 (1936)). This author in fact, contends in his article that germanine while having no influence on the infection itself neutralizes the acantholysis which is primarily present!

Pemphigus ... called,—*pemphigoid-neonatorum* is a superficial ... monkey pox, but which may occur

(epidemically) among babies during the first few days of life.[1] As the skin of these young infants has, as yet, little coherence, new bullae appear at the slightest trauma. This phenomenon—which is also known to exist in epidermolysis bullosa—is called *Nikolsky's phenomenon*.

Since this phenomenon cannot be provoked in healthy babies it must be assumed that the infection entails another (toxic) factor if the skin is actually to get into an acantholytic condition. It is probable that this factor exists also in older children and adults suffering from monkey pox but there, again, the former factor (low coherence of the skin) is lacking.

When pemphigus neonatorum spreads, it may pass into a single, universal "Nikolsky's phenomenon" or *Von Rittersbain's dermatitis exfoliativa* which may end fatally. Microscopic examination shows the process to lie even more superficially than in monkey pox.

Pemphigus epidemicus neonatorum, like pyosis mansoni is highly infectious. No new babies ought to be admitted to a clinic where the disease exists. Unless radical measures are taken at once the disease will take up permanent residence at the clinic in question. A very painstaking search for the cause is imperative more especially it should not be neglected to examine the mothers, the nurses, probationers and maids, and the doctors for any furuncles, sweat-gland abscesses otitis, panaritia, etc. When, in 1922, an epidemic of pemphigus neonatorum broke out in the Basel maternity hospital the source of infection was found to be a laundry maid who had been folding napkins with a whitlow on her hand.

DUDLEY HART in the *British Journal of Dermatology* (1938), described two epidemics which he attributes to rhinorrhoea of a sick child and mastitis of a mother.

At another clinic the disease was found to have spread on account of the babies all being placed on the same clean (!) napkin when weighed. In this case the disease had probably slunk into the clinic via a nurse who was engaged to be married to a man with a classic case of BOCKHART impetigo as it happened, the man also applied to us for treatment at the same time.

[1] Not to be confused with (non-epidemic) syphilitic pemphigus neonatorum.

Although, as already observed, monkey pox is not often found combined with other pyodermata, combinations are nevertheless possible.

An epidemic of pemphigus neonatorum is extremely hard to stamp out. New eruptions appear time after time, wellnigh driving one to



519. Pemphigus vulgaris, not contagious (*Simons-Leyden*)

despair. Despair, however, may give place to fresh courage if one bears in mind that (a) the number of new cases steadily decreases, (b) they occur at ever longer intervals, and (c) finally cease altogether, providing, of course, that general disinfection is not discontinued, not even after the last case has been disposed of (and for one month afterward). For some time after an epidemic of pemphigus

neonatorum no confinement cases ought to be admitted to the infected clinic. Persons—especially personnel—with furuncles, monkey pox, etc. have no place in a maternity hospital: this is a rule to which, for once, there is no exception! The situation which such individuals might create may cost not only a mint of money, but children's lives, as well as the clinic its reputation. This explains why some hospitals have the unenviable name of "harbouring monkey pox".



520 Pyosis mansoni: abscess in the epidermis

PATHOLOGY

The histology of monkey pox clearly shows that the abscess lies in the epidermis, and is not limited to one special dermal organ. The stratum papillare is completely flattened. There is acanthosis. When the abscess is too large for the epidermis it either pushes upwards to the surface, and is clinically visible as a "monkey pock" or pushes the rest of the epidermis—stratum basale—towards the cutis, which, however, it does not penetrate. As the bullae sometimes become fairly large and hang down like small, flaccid bags, it is not improbable that acantholysis is also present.

DIAGNOSIS

Of skin diseases to be differentiated from monkey pox we must mention in the first place *varicella* or chicken pox. The three phenomena distinguishing varicella from monkey pox are, (a) general feeling of illness, (b) irritation, and (c) the central depression in the umbilicated varicella blister

A combination of varicella and monkey pox is far from impossible but the diagnosis however easy theoretically is much more difficult in practice one should indeed, feel quite gratified at its mere possibility Another difference between monkey pox and varicella is that the former appears more regionally—or multiregionally—varicella being more disseminated.

Variola or smallpox *may* resemble either varicella or monkey pox. Like varicella, variola is umbilicated. Variola, however, is coupled with more violent general phenomena. Any difference between variola and varicella can be brought to light by laboratory examination.

Pustulosis vacciniformis is a follicular staphyloderma in which the pustules resemble pock-marks. Many authors apply the term to a slight chicken pox or smallpox infection caught by a child from its brother or sister or at school from class mates that have been vaccinated

Apart from chicken pox and smallpox, monkey pox must also be differentiated from *strophulus* This presents no difficulty if one bears in mind that strophulus is an urticarial affection coupled with itch—which is absent in monkey pox. Strophulus however is infrequent in the tropics See chapter 1

In *urticaria bullosa* too wheals dominate the picture. *Exsudative multiforme erythema* is polymorphous bullae are rare. Its urticarial character too is in evidence

Of tropical skin diseases *pyosis Corletti* and *pyosis Castellani* (called in Ceylon *Kurunegala sore*) should also be mentioned at this point In my opinion both of these are simply monkey pox and/or ecthyma, and surely not pemphigus vulgaris, as DE HAAN (*Arch. Schiffs u. Tropen-Hyg* Vol 7 No 7) asserts. *Pyosis Castellani* is a crusted irritating ecthyma (impetigo) appearing chiefly on the legs. To my mind it is this form which is sometimes seen after mosquito bites The insect's sting causes a local, irritating wheal the patient scratches it and

infects himself, so causing this pyoderma—which, however may also become bullous.

Dermatitis nodosa tropica which does occur among natives (East Africa) is follicular.

Maybe superfluously but for completeness sake, I may here also mention *pemphigus vulgaris* and *dermatitis herpetiformis* or *Duhring's disease*.[1] Both are fairly rare. The former is coupled with general feelings of illness the latter with a general feeling of being "quite fit" which is strikingly incompatible with the spread of the disease. The bullae are very large. Dermatitis herpetiformis is polymorphous it, again, is urticarial in character, and there is severe irritation. There is hypersensitivity to iodine, which, indeed, is of diagnostic value (skin tests with an ointment of 50 % potassium iodide in vaseline)

For the differential diagnosis it is obvious that account must be taken of the possibility that a patient with monkey pox may also have weals

Finally the following dermatoses should be briefly mentioned

Scabies (irritation, typical localization, sometimes cuniculi or burrows) *vesicular eczema* (not—or very rarely—disseminated, erythema weeping) *Sevestre and Jacquet's syphiloid* (vesiculo-erosive napkin dermatitis) *"grain itch"* (urticarial) and, *follicular bullous staphyloderma* (BOCKHART's disease)

THERAPY

To the three characteristic features of pyosis Mansoni already mentioned, I may now add a fourth *i.e.* that monkey pox may soon be cured, given general disinfectant treatment, consistently carried through. This therapy is successful to the point of having diagnostic value. If unsuccessful, then either the patient has not properly carried out the instructions given, or the diagnosis was wrong

The treatment of monkey pox may be summed up as follows — general external disinfection disinfection of clothing if necessary family treatment, and, especially after-treatment. "Family treatment" means that any other members of the patient's household who also have monkey pox, should be treated concurrently

[1] Sometimes called benign pemphigus, which name however had better be avoided.

No other therapy—*e.g.* vitamin injections, dieting, trips to the mountains, irradiation, etc.—will yield any result; if by a lucky chance the patient should recover with such treatment, it will not be because, but in spite of these methods. The preparation of a vaccine takes more time than the treatment itself need occupy and, moreover, a vaccine hardly ever does any good.[1]

Admittedly a stay among the mountains includes much swimming and less sweating, *i.e.* more regular cleansing of the diseased skin and less spreading of the infectious content of the pyosis Mansoni, but the general disinfection can, after all, be carried out far more efficiently at home. Artificial sunlight irradiation for the purpose of destroying the staphylococci *in vitro* will have to be repeated so often if it is to improve the patient's condition at all, that it is bound to do him more harm than good (erythema and desquamation, which facilitate spreading).

In modern times penicillin and the sulphonamides play an important part in the treatment of pyoderma. While being successful in some cases of deep pyoderma, they are not in all cases of superficial pyosis Mansoni, at any rate in such negligible measure that the patient had much better spend his money on proper disinfectants.

Disinfecting treatment of monkey pox consists of frequent bathing. Before the bath the vesicles are opened with a vaccinostyle, and the contents at once thoroughly disinfected.[2] The nails should be well brushed. After the bath, all clothing, as well as the towels used, should be disinfected.[3]

In order to prevent a relapse—which, otherwise, is practically certain to occur—the treatment should be continued for another week.

Ointments are usually not to be recommended in pyosis Mansoni.

Sulphur lotions or liniments which has no maximal dosage, and which are used on account of its disinfecting properties, will give most satisfying results when applied in large quantities.

[1] I would here like to quote DARIER's dictum on the treatment of impetigo: internal treatment [illegible] ineffective. It is a widespread misconception that dieting, medicines [illegible] can help.

[2] It should be remembered that iodine tincture (and soap too, sometimes) may irritate the skin and sensitize it, thereby facilitating the spread of the infection.

[3] Permanganate of potassium in a too weak solution does not disinfect sufficiently; a too strong solution stains the clothes.

The sulphur should be regularly replaced by a fresh quantity (as will naturally happen because of the frequent baths) as otherwise it will turn black and become fetid.

The following "*S-triad*" is a useful guide in treating pyosis Mansoni Sulphur—Soap—Seven days after-treatment.

Some may think the above instructions for the treatment of monkey pox extremely simple and, maybe, dictatorial. But the patient must be treated in a dictatorial manner if he is to follow up the instructions to the letter

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TROPICAL PYOMYOSITIS (BUNG PAGGA)

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DEFINITION

This is usually given as "an acute or subacute inflammation, of uncertain origin, of one or more muscles associated with oedema and at times dermatitis and generally ending in suppuration" The name Tropical Pyomyositis is not altogether a good one because it is doubtful if the condition is confined to the tropics and not all cases go on to the formation of pus By the words uncertain origin" we exclude pyaemic abscess, gumma of muscle, abscesses of muscle occurring in specific fevers haemorrhages in muscles which may suppurate, as in scurvy and those resulting from trauma.

EPIDEMIOLOGY

Though the great majority of cases have been reported from warm countries—East, West and Central Africa (*Bung pagga* is the tribal name for the disease in the northern territories of the Gold Coast) from the West Indies British Guiana, Panama and the Canal Zone, from India and the Far East Java, Japan, Indo-China, the Pacific Islands—they have also been noted on the Continent of Europe, in Paris Vienna and Sweden in fact, the first to be recorded was one by BRUNON in Paris in 1887

According to many authorities the disease is limited to the tropics, at least to warm countries, and is rightly called Myositis or Pyomyositis tropica others among whom are RUGE, DE BARROS, SCHÖNBRUNNER

and HOLM, have recorded it in non-tropical lands also and, therefore, "tropica" is too limiting a term. This leads directly to the question whether these muscle abscesses are of the same origin or nature in the tropics as in temperate climates and in view of the different causes assigned, whether they are the same in the various tropical regions where they are met with.

AETIOLOGY AND PATHOGENESIS

In spite of many investigations having been made the question of aetiology is still undetermined. The organism most often found is *Staphylococcus aureus* this is probably not the primary cause, but a secondary invader converting the myositis into a pyomyositis, the portal of entry being perhaps a mucous membrane, perhaps some small surface wound, such as a furuncle, the organism being carried by the blood-stream to the muscle, in short a septico-pyaemic infection. The same remark probably applies to *Staphylococcus albus* and streptococcus. Two other organisms which have been isolated from these cases deserve special mention, *Pasteurella bouffardi* and *Bacillus serofaciens* BOUFFARD in 1909 isolated from West African patients a Pasteurella which was found also by COMBES at Bamako It was a non-motile, non-sporing Gram-negative bacterium, growing in broth, lactose litmus broth, milk, and on agar but it soon died out and when inoculated into animals it did not reproduce the disease. SCOTT in 1912, described an organism isolated by him from three cases in Jamaica. This was a rod, 1.3–3.5 μ long and 0 6–0 8 μ broad, with square ends but with terminal swelling and involution forms after 4 days growth, aerobic and facultative anaerobic, with, in aerobic conditions a central or subcentral spore motile in vegetative form with peritrichial flagella, the terminal being longer than the lateral. It grew well in broth, with formation of a pellicle which sinks and a fresh one forms and falls, so that a deposit results with clear medium above and sporing forms at the surface gelatin slowly liquefies, litmus milk becomes acid in 4 days on agar it grows as a grey white thin pellicle and cotton wool border stab culture not fir-tree sugars give acid but no gas in glucose, less in saccharose slight in lactose, mannite, raffinose and galactose no change in dulcite. SCOTT did not record any experimental work with this organism.

The only other cause for serious consideration is Filaria. A dead *W. bancrofti* has been most often incriminated or perhaps it would be more correct to say postulated, associated with staphylococcus or streptococcus but rarely has any actual remnant of a filaria been found. The attribution of the disease to filariasis, either *W. bancrofti* or *Loa loa* was due no doubt to the blood examination revealing the presence of



521. Tropical pyomyositis. Oedema in the right lower extremity. (*Gelfand—Southern Rhodesia*)

embryos. These, however, might be merely accidental concomitants, or the condition might be looked upon as a peculiar form of pyaemia with Filaria as a localising factor, a dead filaria supplying the focus for secondary invasion by some pyogenic organism. Others who have made a special study of this point have come to the conclusion that filariasis is not a factor, for the disease occurs where there is no

filariasis. VAUCEL, in 1936 stated that a certain proportion (12 out of 54 of his cases) gave agglutination of *Leptospira icterohaemorrhagiae* but this does not occur in the vast majority Hence, one can at present only agree with ZIEMANN RODENWALDT and others that it is a disease *sui generis* which is, after all, merely begging the question

Endeavour should be made to determine which, if any of the bacteria found—staphylococci, streptococci, pasteurella, the coccobacillus of BOUFFARD, or *Bacillus tetrafaciens*—is actually causative and, finally whether it is a disease *sui generis* or merely a symptom or complication of some other whether it is the same as the *musuma fever* of Samoa, or due to filariasis, or the result of trauma. The subject is one bristling with interesting problems which would well repay research.

SYMPTOMATOLOGY

The onset may be gradual or comparatively sudden at a time when the subject is apparently in excellent health. There is a rise of temperature, rarely above 102 F (38.9 °C) with chills, headache, malaise, pain in a limb at first diffused, over the thigh, or gluteus, calf, deltoid or lumbar muscles—the larger muscles or muscle-groups are usually affected—but in two or three days becoming more localised. Examination reveals some swelling tender and indurated pain is increased on movement. Beyond a certain brawniness there may be no change of the surface, but in some cases there is an *erythema* or even *ecchymosis* Within a week the hard brawny swelling softens and fluctuation is obtained. Puncture at this stage withdraws only clear serous, perhaps blood tinged fluid, with in some cases the organism described above The swelling may now begin to disappear and complete recovery ensue, or on the other hand and particularly if untimely incision has been made the serous fluid becomes purulent and a large abscess with slate-coloured pus forms, the inflammation may extend multiple abscesses develop and the case end fatally

PATHOLOGY

The skin over the muscle affected is firm, brawny not pitting on pressure until later the deeper tissues are oedematous and infiltrated with serous or sero-sanguineous fluid and the muscle itself shows

interstitial and parenchymatous inflammatory changes like those of ZENKER's degeneration. If suppuration has taken place there may be a wall of necrotic tissue enclosing an abscess cavity containing yellow or slate-grey pus in other words according to the stage the fluid may be serous sero-purulent or frankly purulent. The association of thrombophlebitis and tropical pyomyositis is not to be lightly set aside. In the cases observed by GELFAND the arteries were not affected but there may be clot in the veins interfering with blood-supply extension of the inflammation to tissues around the vein and acute necrosis of muscle. It is equally conceivable that the inflammatory process may have begun in the muscle and have affected the vein secondarily

DIAGNOSIS

This rarely presents any difficulty because other conditions associated with deep-seated abscess are usually obvious—osteomyelitis, pyaemia, scorbutic haematoma, embolic abscess in malignant endocarditis, gumma—while the rapidity of development of symptoms would soon eliminate sarcoma in its early stage. The unexplained fever of a week or more may in the tropics especially lead to a suspicion of enteric fever but blood culture and agglutination reactions will exclude this, apart from the rash, the character of the temperature chart and other clinical symptoms. Trichiniasis would be excluded by the history the presence of eosinophilia and the results of muscle biopsy

PROGNOSIS

If the lesion is confined to a single muscle and if the patient is in good general health, and if secondary invasion by pyogenic organisms can be prevented, the outlook is very favourable and the myositis may clear up without any interference. Again, if pus forms and is evacuated while the lesion is localised, the outlook is good, but if other muscles become involved and a pyaemic state develops a fatal issue is almost certain

THERAPY

STEVENTL in 1923 reported excellent results from the use of potassium iodide in doses increasing gradually up to 12 g daily possibly some of his cases were syphilitic gummata, for others who have tried the

same treatment have found it quite ineffectual. VIGORS EARLE, finding the commonest associated organism to be *Staphylococcus aureus* prescribed sulphapyridine in doses of 2 g daily for four or five days (without incision) and reported satisfactory results HUARD and BERTRAND suggest intrafocal staphylococcal bacteriophage where there is suppuration and staphylococcus present in non-suppurative cases they are in favour of diathermy with vaccines and general supportive treatment later after incision, massage to obviate cicatricial contraction with orthopaedic measures if necessary MURRAY LYON made trials of sulphonamide drugs in cases among natives of the Cameroons and the eastern provinces of Nigeria, but observed no benefit—a fact militating against staphylococcus being the basic cause of the condition. It is only fair however to add that DENISON and DICK have stated that half of their cases resolved without going on to abscess formation on their giving sulphathiazole. Antibiotics might be tried though, so far we have seen no account of their use.

The question of incision and evacuation calls for serious deliberation. If carried out in the earlier stage as soon as fluctuation is obtained, there is grave risk of the serous being converted into the purulent and the condition being made worse on the other hand, if postponed there is the possibility of the condition clearing up without surgical intervention. Yet again, if postponed too long there is the fear of the local abscess becoming the focus of a pyaemia which is almost certain to end in death. The best plan to follow would be to thrust in a small exploratory trocar under the strictest asepsis as soon as fluctuation is perceived, but not to open and drain unless pus is obtained

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CHAPTER 27

THE RICKETTSIOSES

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DEFINITION

The rickettsial diseases are a group of illnesses that occur throughout the world. They are caused by the rickettsiae, tiny micro-organisms midway between the bacteria and the filterable viruses, requiring living cells for proliferation, staining poorly with ordinary bacteriological stains, and for the most part transmitted by arthropods. The diseases are characterized by fever, general malaise, joint and muscle pains, headache, eruptions which may be macular erythemas or petechial and haemorrhagic, or vesicular, self limited course varying degrees of immunity varying mortality Epidemic only when the arthropod is a parasite of man.

HISTORY

Although typhus fever (FRACASTORIUS, 1546) was early to be recognised it has only been during the end of the nineteenth century and the beginning of the twentieth that the great variety of rickettsial diseases and their arthropod hosts has been apparent scrub typhus (PALM 1878) Rocky Mountain Fever (WOOD, 1896) fièvre boutonneuse (CONOR and BRUCH, 1910) Brill's disease (BRILL, 1910) murine typhus (NEILL, 1917) trench fever (GRAHAM 1915) Q fever (DERRICK, 1937) rickettsialpox (SHANKMAN 1946). The first proof of arthropod transmission was the transmission of Rocky Mountain spotted fever to man by the bite of a wood tick (McCALLA, 1905), and

in 1909 RICKETTS found organisms in the blood of patients and eggs of ticks

EPIDEMIOLOGY

Ticks are vectors of spotted fever boutonneuse fever tick-typhus of central and eastern Siberia, and to some extent in the transmission of Q fever Rocky Mountain spotted fever of the United States and Canada and the spotted fevers of Mexico Colombia, and Brazil differ only in epidemiological features relating to the different vector species. Kenya typhus, tick-typhus of Abyssinia, and South African tick typhus fever appear to be closely allied if not identical with the earlier described boutonneuse fever of the Mediterranean area. There is suggestion that diseases known as North Queensland tick-typhus and Indian tick typhus are tick borne infections

Mites are vectors of tsutsugamushi disease and of rickettsialpox. They may also be involved in transmission of murine typhus.

The human louse is the vector of epidemic typhus The rat flea is generally regarded as the important vector of murine typhus although a number of other rodent ectoparasites may also be involved. The louse also transmits trench fever

The vector of epidemic typhus is unique among the arthropod transmitting agents of rickettsial diseases in that it feeds exclusively on man No animal source of the disease other than man has been found. Thus the transmission is man louse-man transovarial passage in the louse is not known once infected the louse remains so for a life which is shortened to about 10 days. The inter-epidemic rickettsiae may reside in dried louse feces Fleas can be infected experimentally they remain infected for life and are not harmed but no naturally infected fleas have been found Brill s disease, which is a recrudescence of an old infection with epidemic typhus may represent the last step in the adaptation of rickettsiae to man and may be the reservoir of infection

AETIOLOGY AND PATHOGENESIS

The rickettsiae are small, often pleomorphic, rod shaped to coccoid organisms occurring intracytoplasmically in lice fleas ticks and mites, or sometimes intranuclearly Stain lightly with aniline dyes. Gram-

negative. Non-filterable. Have not been cultivated in cell-free media. Parasites of man and animals, causing diseases that are transmitted by arthropod vectors Classification (*Bergey's Manual of Determinative Bacteriology* 1948) Order *Rickettsiales Gieszczykiewicz*, Family *Rickettsiaceae* Pinkerton, Genus *Rickettsia* da Rocha Lima The type species is *Rickettsia prowazekii* da Rocha Lima.



522. Dermacentor Andersoni
(*Parke Davis Therap Notes* 57 1950)

Key to the species of genus *Rickettsia*

I	Louse-borne	1 Rickettsia prowazekii
II	Flea-borne	2. Rickettsia typhi
III	Tick borne	3 Rickettsia rickettsii
		4 Rickettsia conorii
IV	Mite borne	5 Rickettsia tsutsugamushi
		6. Rickettsia akari

Rickettsiae are characteristically associated with insects and ticks in symbiotic relationship transovarial passage has been proved for some many are known in addition to those pathogenic for man. In recent years the rickettsiae have been considered as a distinct group of

bacteria on the basis of their visibility morphology apparent non filterability and definite metabolic activity which is different in nature from the changes observed in virus infected tissues

Evolution of the pathogenic rickettsiae BURNET (1942) holds that the parasitic organisms have evolved from freeliving forms The first stage was colonization of the gut of primitive insects by saprophytic bacteria some species began to derive nutriment from the cells lining the gut as true parasites, causing damage to the host After a time the host began to tolerate the bacteria as symbiotes within the cells The potential pathogenicity of these bacteria is not lost and may become active when brought into contact with other types of living cells. This contact may arise when the insect host begins living on the blood of a vertebrate which the bacterium is able to parasitize. Since epidemic and murine typhus are not transmitted transovarially in lice and fleas, these rickettsiae may have originated from some common, ancestral, acarine host.

SYMPTOMATOLOGY

In general fever malaise of varying degrees, rash. A lesion develops at the site of the bite of the tick in fièvre boutonneuse, but not in Rocky Mountain spotted fever a lesion develops regularly where the mite bites in rickettsialpox but in tsutsugamushi disease the lesion is more common in Japan than in Malaya and Burma. Mortality is high in epidemic typhus in adults, tsutsugamushi disease and Rocky Mountain spotted fever low in murine typhus nil in trench fever boutonneuse fever Brill s disease and rickettsialpox. Immunity of some degree develops in all.

SUBTYPES

Those tick borne diseases which have not been well studied and in which the causative agent has not yet been named will be discussed here briefly The well known rickettsial diseases are discussed later in detail. For the present Kenya fever and South African tick-typhus are believed to be caused by subtypes of the rickettsia which causes fièvre boutonneuse (Steinhaus)

Tick borne infections possibly related to the spotted fever group exist in Siberia. *Dermacentor nuttalli* is the probable vector in central

RICKETTSIAL DISEASES OF MAN

SUBTYPES

DISEASE	RICKETTSIAL AGENT	VECTOR TO MAN	GEOGRAPHICAL LOCATION	RESERVOIR
I Louse-borne				
Epidemic typhus	*Rickettsia prowazeki*	*Pediculus humanus* var. *corporis* *Pediculus humanus* var. *capitis*	Circum-globular	Man?
Trench fever	*Rickettsia quintana*	*Pediculus humanus* var. *corporis* *Pediculus humanus* var. *capitis*	Europe	Man?
Brill's disease	*Rickettsia prowazeki*	Unknown	United States	Man?
II Flea-borne				
Endemic (murine) typhus	*Rickettsia typhi*	*Xenopsylla cheopis* *Xenopsylla astia*	Circum-globular	Rats, mice
III Tick-borne				
Rocky Mountain spotted fever	*Rickettsia rickettsii*	*Dermacentor andersoni Dermacentor variabilis Haemaphysalis leporispalustris Amblyomma brasiliensis Amblyomma cajennense Amblyomma striatum Amblyomma americanum* and *Ixodes dentatus*	United States, Canada, Mexico, South America	Ticks, rodents, dogs
Fièvre boutonneuse	*Rickettsia conorii*	*Rhipicephalus sanguineus Amblyomma hebraeum Haemaphysalis leachi Rhipicephalus appendiculatus Boophilus decoloratus*	Mediterranean littoral	Ticks, dogs

Continued next page

DISEASE	RICKETTSIAL AGENT	VECTOR TO MAN	GEOGRAPHICAL LOCATION	RESERVOIR
Kenya typhus	*Rickettsia conori*	ditto	East Africa	Ticks, dogs
South African tick typhus	*Rickettsia conori*	ditto	South Africa	Ticks, dogs
Central Siberian tick-typhus	*Rickettsia* — sp	*Dermacentroxenus nuttalli*	Central Siberia	Ticks, rodents, dogs
Eastern Siberian tick typhus	*Rickettsia* — sp	*Dermacentroxenus sylvarum*	Eastern Siberia	Ticks, rodents, dogs
North Queensland tick-typhus	*Rickettsia* — sp	*Ixodes holocyclus*	Australia	Ticks and unknown
Bullis fever	*Rickettsia* — sp	*Amblyomma americanum*	Texas, U.S.A.	Ticks and unknown
Pretibial fever	*Rickettsia* — sp	Unknown	North Carolina, U.S.A.	Ticks and unknown
Australian Q fever	*Coxiella burnetii*	*Haemaphysalis humerosa*, *Ixodes holocyclus*	Australia Mediterranean area	Ticks, bandicoots
American Q fever	*Coxiella burnetii*	*Haemaphysalis humerosa*, *Ixodes dentatus*, *Dermacentor andersoni*, *Dermacentor occidentalis*, *Amblyomma americanum* and *Haemaphysalis leporispalustris*	United States	Ticks and unknown
IV. Mite-borne				
Tsutsugamushi disease	*Rickettsia tsutsugamushi*	*Trombicula akamushi* *Trombicula deliensis* *Trombicula fletcheri*	Eastern and southern Asia, islands of the south west Pacific	Mites, field mice
Rickettsialpox	*Rickettsia akari*	*Allodermanyssus sanguineus*	New York City	Mites, mice

Siberia In eastern Siberia *Dermacentor silvarum* There is a primary eschar fever and rash.

MEGAW (*Indian Med Gaz* 56 (1921) 361) described a spotted-fever like illness resulting from a tick bite. Serologically the causative agent was more closely related to the spotted fever than to the typhus group

In 1944 a spotted fever like disease was recognised in troops in North Queensland the tick *Ixodes holocyclus* was the only one found infesting the troops. Eschar regional adenopathy fever and a maculo-papular rash characterized the disease Rickettsiae were isolated from infected patients by ANDREW *et al* (1946) Sera from patients contained no antibodies against epidemic or murine typhus fièvre boutonneuse South African tick-bite typhus or Rocky Mountain spotted fever Mice and guinea pigs were susceptible.

Bullis fever was first reported by WOODLAND *et al* in 1943 from Camp Bullis in Texas, characterized by fever generalized adenopathy photophobia, marked leucopenia generalized maculo-papular rash and no mortality All cases showed multiple tick bites. A rickettsia was isolated from the ticks *(Amblyomma americanum)* which reproduced the disease in human volunteers.

A rickettsia-like agent pathogenic for guinea pigs was reported by TATLOCK (1944). The guinea pigs had been injected with blood from a patient with "pretibial fever" a new disease first seen in the summer of 1942 at Fort Bragg North Carolina. The disease was characterized by 3 to 5 days of fever splenomegaly a maculo-papular rash typically limited to the legs and rapid recovery No arthropod vector was indicated.

Q fever rarely shows a transient eruption of pink maculo-papules fading with pressure 2 to 3 mm in size scattered on trunk, during first week of fever The main pathology is pneumonitis.

PATHOLOGY

Rickettsiae invade the small blood vessels in typhus and tsutsugamushi disease only the endothelium of the intima, in Rocky Mountain spotted fever also the smooth muscle cells of the media of blood vessels. Reaction of the tissues may be proliferation of the endothelium with infiltration of lymphocytes, plasma cells, large basophilic and acido-

philic macrophages in perivascular arrangement or destruction of tissues following thrombosis of small blood vessels Rickettsiae are at times found in the infiltrating mononuclear cells ALLEN and SPITZ (1945) are of the opinion that more important than the direct damage wrought by the localization of the rickettsiae is the hyperergic effects of the rickettsiae in producing tissue reactions such as fibrinoid degeneration of collagen, necrosis of lymph nodes and spleen, pre dominance of basophilic macrophages and an acute, diffuse, glome rulonephritis which recalls similar tissue reactions in the collagen diseases disseminated lupus erythematosus, periarteritis nodosa and and the arteritis following administration of sulfonamides.

REACTIONS AND PHENOMENA

The Weil Felix reaction Non specific and brought about by the presence of an antigen fraction which is common to the *Proteus* organism and the rickettsiae. In epidemic typhus there is a high *Proteus* OX 19 agglutination titer, a low OX 2 titer and a negative OX K. A rise in titer occurs during the second week of the disease and is insignificant within about 3 months after onset. In endemic (murine) typhus the pattern is about the same as that of epidemic typhus. In Rocky Mountain spotted fever there may be a high titer with either OX 19 or OX 2 but usually not both. In tsutsugamushi disease the Weil-Felix reaction becomes positive for *Proteus* OX K about the 12th to 14th day of the disease, a low titer for OX 19 may occur (sera from louse-borne spirochaetal relapsing fever possess *Proteus* OX K agglutinins) A positive Weil Felix reaction occurs late in boutonneuse fever about the second week of convalescence it may be positive in equal titer for both *Proteus* OX 19 and OX 2

Complement fixation and agglutination reactions: became possible with methods of producing antigen rich in rickettsiae especially from infected yolk-sacs of embryonated eggs Group-specific soluble antigens occur epidemic and endemic (murine) typhus have soluble antigens in common soluble antigens of Rocky Mountain spotted fever are related to those of boutonneuse fever These soluble antigens can be removed from the rickettsial organisms by repeated washing and type specific complement fixing and agglutinating antigens may

be obtained The following can be identified by specific complement fixing or agglutinating antibodies in the sera epidemic typhus, murine typhus, Rocky Mountain spotted fever, boutonneuse fever North Queensland tick typhus, rickettsialpox, tsutsugamushi disease. Specific antigen is now available commercially In the United States testing of suspected sera with specific antigens can be obtained by sending the sera to the State Public Health Service Laboratories or to the National Institute of Health, U.S Public Health Service, Bethesda, Maryland.

THERAPY

Three antibiotics are effective (relief of symptoms occurs within 24 hours and fall of temperature in about 36 hours in the typhus group, Rocky Mountain spotted fever and tsutsugamushi disease) *chloramphenicol* is obtained from filtrates of cultures of *Streptomyces venezuelae* but has since been synthesized *aureomycin* is obtained from *Streptomyces aureofaciens* *terramycin* from *streptomyces rimosus* All are effective orally toxic symptoms are absent except for mild gastro-enteric disturbances with aureomycin orally SMADEL *et al* studied the effect of chloramphenicol in experimentally infected mice, guinea pigs and embryonated eggs they conclude that chloramphenicol has a rickettsiostatic effect in embryonated eggs infected with *R tsutsugamushi* *R. typhi* *R. rickettsii* *R. akari* *R prowazekii* and *R. burnetii* In mice and guinea pigs chemotherapeutic tests against the first four infections also gave evidence of a beneficial effect of the drug Chloramphenicol had only a suppressive effect on the growth of *R. tsutsugamushi* in mice since the infectious agent could be recovered from the tissues of apparently healthy mice which were treated for 100 days after infection. Preliminary observations suggested that the drug may under certain circumstances, sterilize the tissues or cause complete suppression of growth of organisms in mice inoculated with *R. akari* or guinea pigs injected with *R. rickettsii* So far no change in susceptibility of *R. prowazekii* for chloramphenicol has been found as a result of tests designed to detect resistance to the drug

RECENT ADVANCES

Vaccines: satisfactory mass-production of vaccines against epidemic and endemic (murine) typhus and Rocky Mountain spotted

fever by use of infected chick-embryo tissues vaccine against tsutsugamushi disease is still in the experimental stage.

Louse control DDT (dichloro-diphenyl-trichloro-ethane) was proved effective in field trials conducted in Egypt by the United States Typhus Commission in 1942—43 10 per cent. dusting powder controls body and head louse infestation. Other effective agents chordane toxaphene and benzene hexachloride have not been sufficiently studied for toxic effects in man.

Tick repellents dimethyl phthalate, indalone and benzyl benzoate offer considerable protection when applied to clothing New material against the lone-star tick *(Amblyomma americanum)* are N-(*n*-butyl) acetanilide *n*-hexyl ester of mandelic acid beta phenyl beta hydroxy propionic acid, ethyl ester and di-ethylphthalate.

Flea repellents DDT powder kills rather slowly For area control measures chiggers and ticks can be effectively controlled in their natural habitats with dusts or sprays of some of the new insecticides benzene hexachloride chlordane and toxaphene applied at the rate of 2 pounds per acre.

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ROCKY MOUNTAIN SPOTTED FEVER

DEFINITION

MAXCY (1899) describes the disease as follows An acute endemic, non-contagious, but probably infectious febrile disease, characterized clinically by a continuous moderately high fever, severe arthritic and muscular pains and a profuse, petechial eruption in the skin, appearing first on the ankles wrists and back but rapidly spreading to all parts of the body"

Synonyms are *mountain fever black fever blue disease bull fever tick fever of the Rocky Mountains São Paulo exanthematic typhus of Brazil Tobia fever of Colombia spotted fever of Minas Geraes*

HISTORY

First written report by W W WOOD *Report of the Surgeon-General of the Army to the Secretary of War 1896* describing spotted fever in Idaho although it had first been noted in the Snake River Valley of Idaho in 1893 and in the Bitter Root Valley of Montana about 1890 First published report by E. E. MAXCY in the *Medical Sentinel* 1899 In 1902 WILSON and CHOWNING concluded that it was transmitted by the wood tick in 1903 L. P MCCALLA transmitted the disease to man by the bite of infected ticks In 1909 RICKETTS found the rickettsia in the blood of patients and eggs of ticks

EPIDEMIOLOGY

Habitat: infected wood tick *(Dermacentor andersoni)* and the dog tick *(Dermacentor variabilis)*, also rabbit tick *(Haemaphysalis leporis palustris)*, *Amblyomma brasiliensis*, *Amblyomma cajennense*, *Amblyomma striatum*, *Amblyomma americanum* and *Ixodes dentatus*. A number of ticks belonging to the genera *Amblyomma*, *Dermacentor*, *Rhipicephalus*, *Ornithodorus* and *Haemaphysalis* have been experimentally infected. The virus seems to be transmitted by the salivary secretion of the tick, and a tick once infected remains infected for the remainder of life; the virus is transmissible through the ova of the female tick.



523. Rocky Mountain spotted fever
(Armed Forces Inst. of Path.—Washington)

AETIOLOGY AND PATHOGENESIS

The rickettsiae are *minute paired organisms* surrounded by a narrow clear zone or halo and often lanceolate, resembling in appearance a minute pair of pneumococci. Approximately 0.2 to 0.3 micron by 1 micron. Non-motile. Named *Rickettsia rickettsii* (WOLBACH) BRUMPT (*Dermacentroxenus rickettsi* WOLBACH 1919. *Rickettsia rickettsi* BRUMPT

1922. *Rickettsia brasiliensis* MONTEIRO 1931 *Rickettsia typhi* do AMARAL and MONTEIRO 1933 *Dermacentroxenus rickettsi* var *brasiliensis* PINKERTON 1936.) Named for HOWARD RICKETTS. Pathogenic for man, monkeys, and guinea pigs. Rabbits and white rats are moderately susceptible. Animals susceptible in varying degrees include species of ground squirrels, tree squirrels chipmunks, cotton-tail rabbits, marmots, wood rats weasels, meadow mice and deer mice. In Brazil the opossum, rabbit, dog and cavy have been found naturally infected and the Brazilian plains dog capybara, coati and certain bats are also susceptible. Sheep are mildly susceptible.

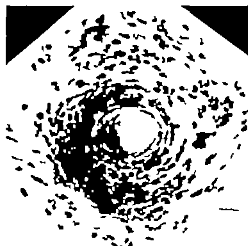


524 Purpura in Rocky Mountain spotted fever

(*Ash and Spitz*)

SYMPTOMATOLOGY

Incubation period of 2 to 12 days after the feeding of the tick onset sudden with chill, pains in bones and muscles, headache photophobia and epistaxis. Following the chill the temperature rises to 102 to 104 F on the second day and continues to rise to 104 to 105 F during the second week with slight morning drops With the recovery the temperature falls at the end of second week by lysis. In fatal cases the temperature may drop to normal and then rise 18 to 24 hours before death which occurs between the 6th and 12th day Pulse ranges from 110 to 140 Respirations 30 to 40 per minute. Rash appears on 2nd to 5th day of fever, first on wrists ankles and back then on forehead, arms legs chest and abdomen. Efflorescence takes 24 to 36 hours At first rose-coloured macules, becoming petechial and even hemorrhagic on a mottled bluish background. Rash fades with fall of fever Nervous symptoms of restlessness and insomnia and after recovery occasionally deafness visual disturbances, slurring speech and mental confusion for a few weeks



525 *R cky M nt n pott d fe er Artery skin of scrotum showing endothelial prolif t nd a smooth muscle fiber containing the parasites.*
(Burt Wolbach)

PATHOLOGY

Skin focal infiltration in walls of arteries necrotic panarteritis and thrombo-arteritis

Kidney: acute glomerulonephritis.
Brain: micro-infarcts in white matter of cortex with cellular infiltrate of lymphocytes, plasma cells and large basophilic and acidophilic macrophages. Rickettsiae found in the cells of the endothelium, smooth muscle of blood vessels, in the nucleus and the cytoplasm.

REACTIONS AND PHENOMENA

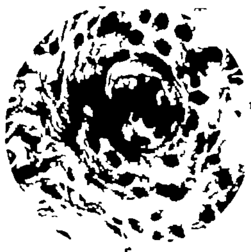
Isolation of the rickettsia by injection of patient's blood intraperitoneally into guinea pigs: a febrile reaction occurs with typical scrotal lesions, involving petechial hemorrhages into the skin, which may become necrotic; rickettsiae found in endothelial cells of tunica vaginalis. *Proteus* agglutinins should be looked for as soon as the disease is suspected and again between the 12th and 15th day after onset; positive agglutinins for *Proteus* OX 19 usually highest, but occasionally those for OX 2 are higher. In some cases none is produced. Specific complement-fixing antibodies begin to appear on about the 8th day and may persist for years. Immunity varies with the severity of the attack. Mortality varies from 20 to 80 per cent.

DIAGNOSIS

Seasonal incidence and restricted distribution eliminate a number of possibilities. Cerebrospinal fever and measles are the two diseases most liable to be temporarily mistaken for Rocky Mountain spotted fever but the latter does not have the neck rigidity of cerebrospinal fever nor the coryza and lacrimation of measles. The rash of typhoid fever is more palpable and elevated and generally more restricted to the trunk. The Weil-Felix test aids in limiting the probable diagnosis to the rickettsial group, the complement fixation test will differentiate spotted fever from epidemic typhus, endemic (murine) typhus, Q fever, tsutsugamushi disease and boutonneuse fever.

THERAPY

Intravenous plasma and whole blood for peripheral circulatory collapse; hypnotics as necessary to prevent exhaustion from restlessness. Para-aminobenzoic acid is valuable in large doses: 0.5 to 1.0 g per pound of body weight per day to produce blood levels of from 30 to 60 mg of PABA/100 ml; stop if acidosis or leukopenia occur. Fever



526. Rocky Mountain spotted fever Artery skin of scrotum (human case) showing endothelial proliferation and a smooth muscle fiber containing the parasites. *(Burt Wolbach)*

ROCKY MOUNTAIN SPOTTED FEVER
Effect of **CHLOROMYCETIN**
Therapy on Duration of Fever

PRETREATMENT
TREATMENT
15 TREATED CASES
46 CONTROLS
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
DAYS OF FEBRILE REACTION

527 Therap Notes 57–1950 *(Parke Davis)*

lasts about 6 days after starting PABA by mouth. If available, aureomycin, chloramphenicol or terramycin given orally will effect amelioration of toxicity symptoms and rash in 24 to 48 hours and the patient is convalescent about third day. Initial dose is 60 mg/kg/body weight divided into three doses at hourly intervals, followed by 0.25 to 0.5 g every three hours.

RECENT ADVANCES

Vaccination by phenolized emulsion of tick or chick-embryo virus gives a significant protection for about one year. Such vaccines are produced by the Rocky Mountain Laboratory of the U.S.P.H.S., Hamilton, Montana. If contact with ticks during their season of feeding cannot be avoided, then clothing as recommended for protection against tsutsugamushi disease should be used. Chloramphenicol or aureomycin might give protection if given prophylactically.

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TRENCH FEVER

DEFINITION

A specific, relapsing, infectious disease transmitted from man to man by the body louse *Pediculus humanus corporis*. There is evidence that the disease is rickettsial in origin but this has not been definitely proved. Blood and urine are infectious over a long period.

Synonyms are *Wolhynian fever quintan fever Polish fever Russian intermittent fever Meuse fever His Werner disease gaiter pain fever shin fever shank fever*

HISTORY

First published by GRAHAM in *Lancet* for the year 1915 Original source believed to be somewhere in Russia and from there spread to all battle fronts in Europe by German and Austrian troops as they moved from one battle front to another Caused about one-third of the morbidity of the troops of World War I



528 Pediculus pubis and pediculus corporis, capitis or vestimenti

EPIDEMIOLOGY

Habitat the epithelial lining of the gut of the body louse *(Pediculus humanus var corporis)* where they occur extracellularly and *Pediculus capitis* The virus is not transmissible through the ova the louse remains infected throughout its span of life The disease has been reproduced in human volunteers by inoculation with blood, urine and sputum from infected patients Man becomes infected by way of infected fæces rubbed into the skin or by inhalation of them.

AETIOLOGY AND PATHOGENESIS

Coccoid or ellipsoidal organisms often occurring in pairs more plump and staining more deeply with Giemsa stain than *Rickettsia prowazeki*

DA ROCHA LIMA gives their size as 0.2 to 0.4 by 0.3 to 0.5 microns. In lice appear as short rods frequently in pairs and often bipolarly stained. Named *Rickettsia quintana* SCHMINKE. (*Rickettsia wolhynica* JUNGMANN and KUCZYNSKI 1918 *Fessilis quintana* suggested as a possible subspecies "if necessary" by MEGAW 1943). Has not been cultivated on tissue culture or any cell-free medium, though *Rickettsia pediculi* considered by some identical with *Rickettsia quintana* has been cultivated on human and horse blood agar. Pathogenic for man, causing recurrent fever. No strain has been definitely established in laboratory animals.

SYMPTOMATOLOGY

Incubation period of 14 to 60 days. Occasional prodromata of headache, pains in legs, slight fever, onset sudden with headache, dizziness, pains in legs and back and behind eyeballs, conjunctivae injected. Rash appears early or late, often in crops lasting 24 hours, pink macules or papules 2 to 4 mm, fading with pressure on chest, back and abdomen. Fever, not definite pattern, less than one week with a sharp rise for a few days, or 6 to 7 weeks with relapses not distinctly marked, or regularly relapsing with normal intervals of 5 to 7 days. May be from 3 to 7 relapses. Usually there is complete recovery in 5 to 6 weeks from time of onset. Spleen enlarged and hard in about 80 per cent.

PATHOLOGY

Exanthem shows perivascular lymphocytic and polymorphonuclear infiltration, no necrosis of blood vessels.

REACTIONS AND PHENOMENA

Partial immunity is produced after an attack of the disease. Relapses may occur as long as two years after the initial attack. Second attacks have been produced experimentally four or five months after the first attack. Individuals who have had trench fever may infect lice up to at least 443 days after the onset of the disease. Weil Felix reactions negative.

DIAGNOSIS

From influenza by the scarcity of respiratory signs, hardness of the

spleen, areas of pain and tenderness and relapsing character of the fever From typhoid by the more sudden onset absence of intestinal symptoms and typhoid bacilli From malaria by the irregularity of the fever rash, tender areas and absence of malarial parasites From spirochetal relapsing fever by the irregularity of the fever although the onset, pains and rash are somewhat similar Both liver and spleen are enlarged in relapsing fever From dengue fever by the lack of leukopenia and longer course. From typhus in that the rise of fever is abrupt and not ladder-like, less toxicity and the rash is not petechial

THERAPY

Symptomatic for the severe abdominal and muscle pains usually acetyl salicylic acid suffices No record as yet of the use of *para*-aminobenzoic acid, aureomycin or chloramphenicol, but success in suppressing the symptoms of the disease is to be expected

RECENT ADVANCES

Control is effective by eradicating the louse population—see control of epidemic typhus

LITERATURE

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ENDEMIC (MURINE) TYPHUS

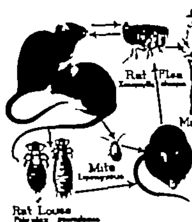
DEFINITION

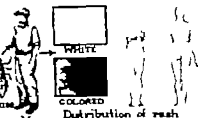
A relatively mild rickettsial disease of 9 to 15 days duration characterized by headache and a rash, transmitted to man by the rat flea. *Shop typhus* is the name given to this disease in Malaya, *flea typhus rat typhus tabardillo Mexican typhus*

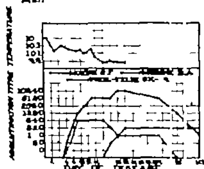
HISTORY

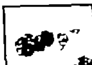
Although an endemic and sporadic form of typhus fever had been recognized in Europe the southern United States, Mexico and Australia for many years the first indication of its difference from epidemic

EPIDEMIOLOGY OF THE RICKETTSIAL INFECTIONS
TYPHUS FEVER
ENDEMIC OR MURINE TYPHUS








ENDOTHELIAL CELLS FROM THE TUNICA OF GUINEA PIG CONTAINING RICKETTSIAE. (NEILL-MOOSER [illegible])

Epidemiology—
Reservoir: common rat and other rodents; diseases associated with rat harbors; common among workers of food handling establishments; transmission from person to person by contact not observed; prevalent summer and fall. Casee poradic

Clinical F ture —
Less severe than epidemic typhus case fatal ty rate ± 3 per cent

Prevention—
Control of the rat population by trapping, poisoning and rat-proof ng

GEOGRAPHIC DISTRIBUTION



[illegible] TYPHUS FEVER

typhus fever was the observation of a scrotal reaction in guinea pigs infected with endemic typhus by NEILL (1917) MOOSER (1928) confirmed this and also described the rickettsiae in the tunica vaginalis of the guinea pig MAXCY (1926) excluded transmission of the sporadic forms by lice and DYER *et al* (1931) found the rickettsiae in rat fleas MOOSER (1931) found the infection in rats Antigenic differences between epidemic and endemic typhus have since been demonstrated.

EPIDEMIOLOGY

Habitat infected rat fleas *(Xenopsylla cheopis Xenopsylla astia)* infected chicken fleas *(Echidnophaga gallinacea)* found on wild rats, and the rat louse *(Polyplax spinulosus)* Wild rats and field mice act as the reservoir of infected feces rubbed into the skin or inhaled. The human louse *(Pediculus humanus corporis)* is capable of transmitting the infection from man to man epidemics are possible by louse transmission. Human cases are commonest in tropical and subtropical climates where rats and fleas are numerous, especially near wharves granaries and store houses.

AETIOLOGY AND PATHOGENESIS

The rickettsiae resemble *Rickettsia prowazeki* in morphological and staining properties Non motile Gram negative.

Named *Rickettsia typhi* (WOLBACH and TODD) PHILIP (*Dermacentroxenus typhi* WOLBACH and TODD 1920 *Rickettsia manchuriae* KODAMA, TAKASHI and KONO 1931 *Rickettsia mooseri* MONTEIRO, 1931 *Rickettsia exanthematofebri* KODAMA, 1932 *Rickettsia muricola* MONTEIRO and FONSECA, 1932 *Rickettsia murina* and *Rickettsia fletcheri* MEGAW 1935 *Rickettsia prowazeki* var *mooseri* PINKERTON 1936 *Rickettsia prowazeki* sub-species *typhi* PHILIP 1943 *Rickettsia typhi* PHILIP 1943) Pathogenic for man, apes, monkeys rabbits, guinea pigs white rats eastern cotton rats, white mice, gerbils. Other susceptible animals include the woodchuck house mouse meadow mouse, whitefooted mouse old field mouse cotton mouse golden mouse, wild rat *(Rattus norvegicus)* wood rat, rice rat, flying squirrel, gopher cotton-tail rabbit swamp rabbit chipmunk skunk opossum and cat After intra-peritoneal inoculation into guinea pigs a characteristic reaction occurs with testicular swelling without ulceration.

SYMPTOMATOLOGY

Incubation period of 6 to 14 days. May be prodromal symptoms of headache backache arthralgia for 1 to 3 days Onset usually sudden with chill, headache, and fever within several hours the temperature climbs for 3 to 4 days without remission, then is continuous or with mild morning remissions between 103 F to 104 F for about 12 days defervescence by lysis in 3 days. Rash generalizes quickly on upper abdomen, shoulders, arms and thighs rarely on face, palms and soles The lesion is indistinct, pea-sized, fades with pressure for the first few hours, may then become papular starts about 5th day of fever and lasts about 5 days. Transient partial deafness, weakness and debility for variable periods may follow severe courses. Recovery is complete.

PATHOLOGY

In general similar to that of epidemic typhus not known in detail since fatalities are uncommon. Cutaneous petechiae are infrequent and large areas of skin necrosis have not been reported.

REACTIONS AND PHENOMENA

Prolonged immunity in man and animals following infection. Complete cross immunity between epidemic and endemic typhus in guinea pigs recovered from infections with *Rickettsia prowazeki* and *Rickettsia typhi* No cross immunity between endemic typhus and Rocky Mountain spotted fever Q fever or tsutsugamushi disease in guinea pigs. Distinguishable from the rickettsiae of spotted fever Q fever and tsutsugamushi disease by complement fixation, agglutination and precipitin tests, less readily from *R prowazeki* by these tests. Has common antigenic factor with *Proteus* OX 19 and soluble antigen in yolk-sac cultures

DIAGNOSIS

From typhoid fever by the more sudden onset in endemic typhus, more cutaneous lesions which do not fade with pressure after the first few hours the shorter course, negative Widal reaction, and negative blood culture. In children from infectious mononucleosis by the lack of enlarged lymph nodes angina, abnormal leukocytes and negative heterophile antibody reaction. From boutonneuse fever the

absence of the "tâche noire" and regional adenitis From meningococcemia by blood culture and spinal fluid findings

THERAPY

See treatment of epidemic typhus

RECENT ADVANCES

In serological studies on soldiers who had been immunized with epidemic typhus vaccine and at a later date contracted endemic typhus it was found that the complement fixation titers were as high with epidemic as with endemic antigen however the sera of such persons gave higher titers with the endemic antigen when tested by the agglutination technique Measures for control of endemic (murine) typhus in the United States have been directed exclusively against the reservoir of the disease and its vectors. Vaccines have been prepared but so far are relatively untried Temporary control of rat ectoparasites by dusting rat runs and harborages with 10 per cent DDT powder Permanent control by rat proofing of buildings, rat destruction and good general sanitation.

LITERATURE

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RICKETTSIALPOX

DEFINITION

An acute non-fatal rickettsial disease characterized by an initial skin lesion followed by chills fever and a papulo-vesicular rash transmitted to man by a rodent mite. A synonym is Kew Gardens spotted fever

HISTORY

First published by SHANKMAN in the *New York State Journal of Medicine* 1946 but also described independently by HUEBNER, STAMPS and

ARMSTRONG (1946), who named the disease rickettsialpox, and by SUSSMAN (1946). First reported in New York City and recognised as a new disease caused by an undescribed rickettsia and transmitted by a previously unsuspected vector

EPIDEMIOLOGY

Habitat blood of human cases and an ectoparasite of rodents the mite (*Allodermanyssus sanguineus* HIRST) A total of 332 cases has so far been reported, all from 4 Boroughs in New York City Rickettsiae were recovered from pools of mites collected in the housing developments where the disease occurred The mites have been shown to be able to transmit the disease to normal mice by feeding on them. Transmission to man by mites has not been effected, and it is not known if transmission is by way of the bites of the mites or by way of their infected feces Identical strains have been isolated from patients, mites and mice. The initial lesion has the appearance of a bite. The mouse and the mite were found in close proximity to the cases of rickettsialpox.



530. Primary lesion of rickettsialpox.
(Rose—New York)

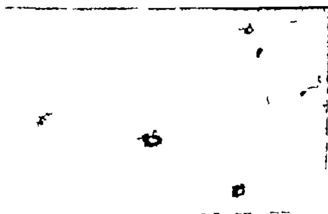
AETIOLOGY AND PATHOGENESIS

Minute diplobacilli occurring intracellularly and extracellularly and bipolarly stained rods Resemble typical rickettsiae morphologically Non-motile Gram negative. Stain well by Machiavello s method, the organisms appearing bright red against a blue background. Named

Rickettsia akari HUEBNER, JELLISON and POMERANTZ. From *Acarus* a genus of mites. Pathogenic for man. Experimental infections have been produced in white mice and guinea pigs by the inoculation of infected blood (irregularly), and of infected liver and spleen suspensions infected brain lymph nodes tunica washings and by infected yolk-sacs. Symptoms in mice include inactivity accelerated respiration, ruffled fur with occasional deaths in guinea pigs fever and marked scrotal reactions. Infected embryos are killed in 4 to 7 days It has not been found pathogenic for monkeys

SYMPTOMATOLOGY

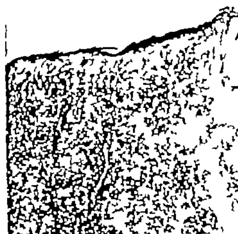
The initial lesion is a small erythematous, non-tender non-itching papule which is followed in 3 or 4 days by regional adenopathy it



531 Rickettsialpox secondary lesions with vesiculation. *(Ross—New York)*

continues to develop and reaches its maximum size about the second or third week of fever when it is 1.5 to 2 cm in diameter and has passed from a vesicular to a scabbed stage Fever occurs suddenly with chills and headache about one week after the appearance of the initial lesion. Within 24 to 72 hours there appears a generalized eruption coming in crops first on the trunk or face later on the extremities, occasionally on the soft palate and tongue but rarely on palms and

soles. The fever is remittent or intermittent up to 103.5 to 105 F and lasts about 7 days There are muscular pains lassitude, photophobia. Enlargement of the spleen, and generalized lymphadenopathy is uncommon. The fever falls by lysis One month after recovery the initial lesion persists as a pigmented area, and the regional lymph nodes are still palpable.



532. Rickettsialpox. Edge of the primary lesion. Partial necrosis and collapse of the epidermis at the right. Dermal inflammatory changes and necrosis.

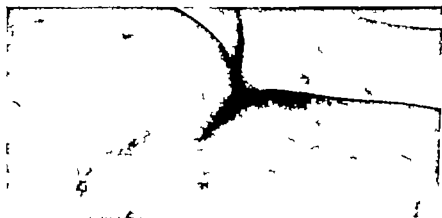
PATHOLOGY

The pathological picture in man is unknown since there have been no deaths The primary lesion shows necrosis of the epidermis and coagulation necrosis of the adjacent dermis necrosis of capillaries and agglutinative thrombi and small haemorrhages in a few areas. The infiltrate is largely lymphocytic and mononuclear

REACTIONS AND PHENOMENA

Antigen prepared from infected yolk-sacs are highly specific except for cross reactions with Rocky Mountain spotted fever antigens Sera from convalescent patients fixed complement with the homologous antigen and usually with Rocky Mountain spotted fever antigens though at a lower titer Does not have a common antigenic factor

with *Proteus* strains except that low titers were obtained in a few recovered cases in agglutination tests with *Proteus* OX 19 Guinea



533 Secondary rash of rickettsialpox.

(Rose—New York)

pigs recovered from rickettsialpox are immune to infection with strains isolated from infected mites



534 Rickettsialpox Secondary lesion. View of typical vascular lesion A thrombus plugs the lumen The perivascular cuffs are necrotic and partially fragmented.

(United States Public Health)

DIAGNOSIS

From varicella by the initial lesion and past history of chicken pox from variola by its lack of predilection for exposed areas of the skin and its mild course from infectious mononucleosis by the lack of characteristic blood picture and negative heterophile antigen reaction from endemic typhus by the vesicular character of the eruption from Rocky Mountain spotted fever by the difference in distribution and in character of the eruption.

THERAPY

Smadel reports that chloramphenicol is effective in experimental infection in mice and that complete suppression of the growth of the organisms was possible. Rose reports that in two patients treated with aureomycin (1 0 gram orally at six hour intervals) the temperature was normal within 24 hours the rash faded and symptoms disappeared.

RECENT ADVANCES

See endemic (murine) typhus for rodent and mite control.

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TSUTSUGAMUSHI DISEASE

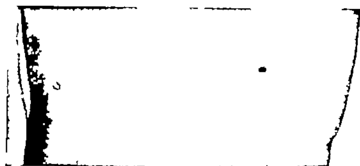
DEFINITION

An acute rickettsial disease transmitted to man by the bite of the larval kedani mite characterized by region lymphadenitis fever of two weeks duration, macular eruption on the face chest, extremities and trunk The above Japanese name is the oldest.

Synonyms are *scrub typhus mite typhus Japanese river fever tropical typhus Shimamushi Kedani mite disease flood fever Sumatran typhus Malayan scrub typhus Queensland coastal fever*

HISTORY

First published by THEOBALD A. PALM in the *Edinburgh Medical Journal* 1878 although described by the Japanese about 1810 Little known outside of Japan prior to 1942 when jungle warfare increased the



535 Primary lesion of scrub typhus or tsutsugamushi fever
(*Allen and Spitz*)

population exposed. During World War II approximately 6,685 cases among U S Army personnel in contrast to 64 cases of epidemic typhus.

EPIDEMIOLOGY

Habitat the mites (*Trombicula akamushi Trombicula deliensis* syn. *T walchi Trombicula fletcheri* and probably several others) Infective through the ova of the adult female. Only the larvae feed on rodents or man Reservoir hosts are probably wild rodents including the house and field rats mice and voles and probably some birds.

AETIOLOGY AND PATHOGENESIS

The rickettsiae are pleomorphic bacterium-like micro-organisms, ellipsoidal or rod-shaped often appearing as diplococci or short bacilli with bipolar staining diffusely distributed in the cytoplasm of the cell. Size 0 3 to 0 5 by 0 8 to 2 microns Named *Rickettsia tsutsugamushi* (HAYASHI) OGATA (*Theileria tsutsugamushi* HAYASHI 1920 *Rickettsia orientalis* NAGAYO TAMIYA MITAMURA and SATO 1930 *Rickettsia akamushi* KAWAMURA and IMAGAWA 1931 *Rickettsia orientalis* var *schüffneri* do AMARAL and MONTEIRO 1932 *Rickettsia megawi* do AMARAL and MONTEIRO 1932 *Rickettsia pseudotyphi* VERVOORT 1938

Rickettsia sumatranus [*sic*] KOUWENAAR and WOLFF 1939 *Dermacentroxenus orientalis* MOSHKOVSKY 1945) From two Japanese ideographs transliterated *tsutsuga* something small and dangerous, and *mushi* a creature now known to be a mite Pathogenic for man



536 Tsutsugamushi disease, rash and ulcer

monkeys, gibbons, guinea pigs, hamsters, rats voles, mice gerbils rabbits (by intraocular injection) and chick embryos. There is a wide variation in the virulence of different strains for laboratory animals infection being established with great difficulty with some, while others may cause a high mortality

SYMPTOMATOLOGY

Incubation 12 to 18 days a primary lesion at site of mite bite, vesicle—necrotic ulcer—eschar is common in Japanese strains, less frequent in scrub typhus Three days later onset abrupt headache, backache chills fever nausea, vomiting Fever increases the first week to 105 elevated until lysis during second to third week. Pulse slow first week, increases second week May be convulsions coma, palsies nystagmus neural deafness, cough, dyspnoea, cyanosis, splenomegaly Eruption begin 4th to 5th day macular or papular first on trunk and then to extremities lasts 3 to 7 days fades on pressure.

PATHOLOGY

Disseminated focal vasculitis and perivasculitis of the smaller vessels consisting of accumulations of monocytes plasma cells and lymphocytes

REACTIONS AND PHENOMENA

Rickettsiae may be recovered by inoculation of mice with blood of patient during febrile period Mice die in 10 to 20 days smears from peritoneum or spleen stained by GIEMSA method show intracellular organisms Antigens from different strains vary in sensitivity when



537 Widespread eruption of tsutsugamushi fever (*Ash and Spitz*)

tested by complement fixation with immune sera. There are probably a number of different types on the basis of complement fixation with immune sera Has a common antigenic factor with *Proteus* OXK. Immunity conferred by infection appears less complete than in typhus and Rocky Mountain spotted fever Relapses may occur Blood counts show leukopenia Fatality rate 10 to 20 per cent

DIAGNOSIS

History of exposure in endemic areas the primary lesion and regional lymph nodes help to differentiate it early Systemic signs of headache, fever relative bradycardia and leukopenia are common to other rickettsial diseases and to dengue, malaria, infectious hepatitis and typhoid. The rash does not become petechial as in typhus or Rocky Mountain spotted fever and it appears about 2 days later.

RECENT ADVANCES

Control measures are aimed at the mite vector The U.S Army anti-mite fluid used for impregnating clothing consists of benzyl benzoate and dibutyl phthalate plus an emulsifier Clothing dipped in this emulsion and allowed to dry remains miticidal after prolonged washing in fresh or salt water If soap is used the material must be applied every three washings The ground is disinfected by cutting all vegetation level to the ground applying diesel oil every second day for several weeks until the ground dries sufficiently to kill all the mites Chloramphenicol in small doses will protect persons exposed in highly endemic areas so long as the drug is given, but signs of infection may appear after the drug has been discontinued. Large doses may result in non-infection.

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FIÈVRE BOUTONNEUSE

DEFINITION

A mild rickettsial disease transmitted by the brown dog-tick, characterized by a "tache noire" regional adenopathy a rash which appears first on the trunk and may subsequently involve the entire body Low mortality

Synonyms are *Fièvre escharonodulaire exanthème typhoide estival de thrombodermite aiguë exanthème infectieux épidémique eruptive fever Marseilles* or *Mediterranean fever fever of Conor and Bruscb*

HISTORY

First published by CONOR and BRUSCH in the *Bull soc path exotique* 1910 First described in Tunisia, but was later observed in the Mediterranean basin including Spain, Marseilles, Italy Rumania, Greece Egypt and the North coast of Africa. May be related to the tick-bite typhus of Kenya, Abyssinia, and South Africa.

EPIDEMIOLOGY

Habitat the brown dog-tick *(Rhipicephalus sanguineus)* and also the ticks *Amblyomma hebraeum Haemaphysalis leachi Rhipicephalus appendiculatus* and *Boophilus decoloratus* Transmissible through the ova of adult female ticks The probable animal reservoir is the dog The virus is found in all the tissues of the tick and survives in the tick for as long as 18 months undergoes transovarial passage.

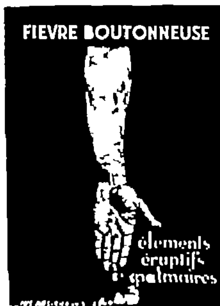
AETIOLOGY AND PATHOGENESIS

In the tick diplococcoid and diplobacillary forms predominate, though when the rickettsiae occur in compact masses they are smaller and more coccoid In tissue cultures the organisms are lanceolate, diplococcoid and diplobacillary occurring in the nuclei as well as in the cytoplasm of cells Size 0.3 to 1 4 by 1 to 1 75 microns Stain purplish with Giemsa stain. Gram-negative. Non motile. Pathogenic for man and guinea pigs It is also pathogenic in varying degrees for dogs, horses spermophiles, monkeys rabbits, gerbils and white mice Named *Rickettsia conori* BRUMPT (*Rickettsia megawi* var *pijperi* do AMARAL and MONTEIRO 1932 *Rickettsia blanci* CAMINOPETROS, 1932 *Dermacentroxenus rickettsi* var *pijperi* MASON and ALEXANDER, 1939 *Dermacentroxenus rickettsi* var *conori* MASON and ALEXANDER, 1939 *Dermacentroxenus conori* STEINHAUS, 1946)

SYMPTOMATOLOGY

Incubation 5 to 6 days primary lesion at site of tick bite in 50 to 80 per cent of cases an indurated, hyperemic, painless papule or ulcer

with regional lymphadenitis Onset abrupt with chill, headache gastric distress pains in joints. Fever irregular often above 104 °F with morning remissions lasts 12 to 14 days and subsides by lysis. Eruption begins 3 to 4 days after initial chill a maculopapular rash first on abdomen spreading rapidly to extremities palms and soles changes from hyperemic to hemorrhagic and at times ulcerous nodules fades with defervescence Stupor delirium and meningeal symptoms usually absent. Case fatality rate less than 3 per cent.



538.

PATHOLOGY

Sections of the maculopapular rash show hyperplasia of vascular endothelium, lymphocytic and monocytic perivascular infiltrations, affecting the papillary and subpapillary vascular plexuses. In guinea pig tissue the rickettsiae are found in peritoneal serosal cells macrophages endothelial and smooth muscle cells of blood vessels usually in pairs, staining deeply with Giemsa s fluid lanceolate in shape, often with narrow clear halo

REACTIONS AND PHENOMENA

The disease is related immunologically to Rocky Mountain spotted fever with which it cross-immunizes, but the spotted fever vaccine does not protect against the Mediterranean or South African strains. Distinguishable from *Rickettsia rickettsii* by specific complement fixation. Has a common antigenic factor with *Proteus* OX 19 and OX 2.

DIAGNOSIS

Clinically fièvre boutonneuse can be distinguished from typhus by the *tâche noire* followed by scab formation the regional adenitis,



539

the character of the eruption seasonal distribution, mild character of the disease and the absence of lice. Rickettsiae can be found in the endothelial cells of the bone marrow by sternal puncture during the period of fever and by inoculation in guinea pigs by the intraperitoneal route after an incubation period of 3 to 6 days there is a rise of temperature to 104 to 105 F for four to six days marked scrotal swelling with tunica adherent to the scrotal sac, rickettsiae may be found in serosal smears.

THERAPY

No reports are yet available as to the use of *para*-aminobenzoic acid, chloramphenicol or aureomycin but success with these measures is to be expected. The mild character of the disease warrants only supportive therapy to relieve symptoms of headache, joint pains nausea and vomiting



540 [illegible] boutonneuse. The histology is identical with that of rickettsial pox and tsutsugamushi fever

RECENT ADVANCES

Control measures as outlined for tsutsugamushi disease Ticks on dogs can be controlled by DDT 10 [illegible] dusting powder

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EPIDEMIC TYPHUS

DEFINITION

Typhus is an acute rickettsial disease transmitted in epidemics by the body louse, characterized by sudden onset, continuous high fever terminating by rapid lysis after about fourteen days, a generalized macular eruption tending to become hemorrhagic on trunk and limbs, but avoiding the face, a delirium which may pass into a fatal coma, and a tracheobronchitis often followed by pneumonia. The mortality



541 Petechial rash in epidemic typhus. *(Wolbach—Boston)*

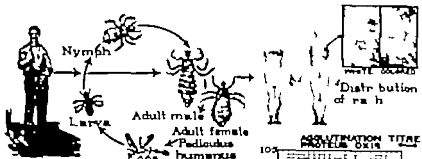
has varied greatly in different epidemics, from as low as 5 to 10 per cent. to as high as 70 per cent.

Synonyms are *Jail fever, war fever, famine fever, ship fever, hospital fever, petechial fever, morbus pedicularis, tabardillo y puntos, pintas, febris purpurea epidemica, febris quam lenticulas vel puncticulas vocant, morbus hungaricus, la pourpre, pipercorn, febris petechialis vera, febris maligna pestilens, typhus carcerorum, morbus castrensis, typhus exanthematicus, Faulfieber, Hauptkrankheit, dermotypho, tabardillo, Fleckfieber, Irish ague*

EPIDEMIOLOGY OF THE RICKETTSIAL INFECTIONS

TYPHUS FEVER

EPIDEMIC OR HUMAN TYPHUS



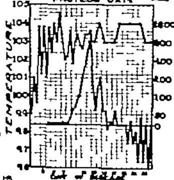


Infection infurious to louse

Copro contamin tion by crushing or cont minat on of b t wound

Rats and mice—low susceptibility

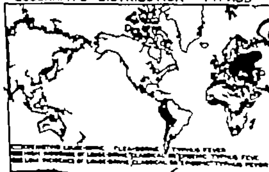
Gu nea pig—scrotal involvement rare



Epidemiology—Disease of dirt and bad sanitation, autumn and winter months, poverty and overcrowding favorable to louse transmission very contag ous.

Prevent on—Vaccination with Cox chick embryo vaccine. Louse prophylaxis with insect de DDT

GEOGRAPH C DISTRIBUTION—TYPHUS



CLINICAL FEATURES

Incubation period 4-14 days, onset 2 days Headache, nausea delirium; face and eyes congested, stuporous drunken expre sion; tongue coated

Urine—cloud of albumin, decrease of urea and chlorides.

Rash—Fifth day on abdomen then chest and back of trunk pleomorphic mulberry, petechial persist for 10 days, fades slowly

Pulmonary complications parotitis

Mortality up to 60 per cent

HISTORY

At the end of the fifteenth century typhus fever was prevalent in many parts of Europe the first scientific account comes from the pen of HIERONYMUS FRACASTORIUS *De contagione* Venice, 1546 who had an opportunity to observe the disease during the epidemics in Italy in 1505—8 and who described it as a disease indigenous to Cyprus and the neighboring islands and appearing for the first time in Italy Severe epidemics of typhus have occurred during practically every great war in Europe. In the sixteenth century typhus became epidemic in Mexico and in the nineteenth century it appeared in certain centers in the United States and Canada. The role of the body louse in transmitting the disease was demonstrated by NICOLLE, COMTE and CONSEIL in 1909 In 1910 RICKETTS and WILDER described the rickettsia in the blood of individuals ill with typhus and in lice that had fed on typhus patients DA ROCHA LIMA (1916) named the organism *Rickettsia prowazeki* in honor of RICKETTS and PROWAZEK, both of whom died while investigating typhus fever

EPIDEMIOLOGY

Habitat the body louse *(Pediculus humanus* var *corporis)* head louse *(Pediculus humanus* var *capitis)* Experimentally other insects have been found capable of harboring and transmitting the organism the monkey louse *(Pedicinus longiceps)* the rat flea *(Xenopsylla cheopis)* and transmissions from rat to rat have been obtained by *Polyplax spinulosa* *Rickettsia prowazeki* occurs in the blood of patients during the febrile period and up to 10 days after the symptoms have disappeared the louse becomes infected by sucking blood from them. Rickettsiae are found in the cells of the intestinal tract of the louse, but not in the salivary glands Great numbers of rickettsiae are discharged in the excreta. Transmission occurs by contamination of the bite puncture or abrasions of the skin, the conjunctivae or respiratory mucous membranes by crushed lice or infected louse-feces. Dried louse feces may constitute the reservoir of infection during interepidemic periods Typhus is a disease of cold weather because the clothing that protects man also protects the louse

AETIOLOGY AND PATHOGENESIS

In smear preparations the rickettsiae appear as minute coccoid or

rod-shaped organisms, frequently in pairs, sometimes in long chains, with a diameter of 0.3 microns the electron microscope shows a limiting membrane with numbers of dense granules in the protoplasm. Named *Rickettsia prowazeki* DA ROCHA LIMA, (*Rickettsia exanthematotyphi* KODAMA, 1932 *Rickettsia prowazeki* var *prowazeki* PINKERTON, 1936 *Rickettsia prowazeki* sub-species *prowazeki* PHILIP 1943). Pathogenic for man, apes, monkeys, guinea pigs, cotton rats, gerbils the louse (*Pediculus humanus*) Inapparent infections occur in white mice, white rats and rabbits.

SYMPTOMATOLOGY

Incubation period of 5 to 15 days onset sudden with severe headache which persists, giddiness, generalized aches and pains During the first 2 or 3 days the temperature keeps rising to reach a height of 103 to 104 °F where it remains until death or recovery remissions appear about the 10th to 12th day with rapid decrease to normal on about the 14th day The pulse is rapid in proportion to the temperature. With the appearance of the rash, symptoms become aggravated cardiac weakness increased respiratory rate, cough, delirium or stupor deafness. The rash appears between the 4th and 7th day as macules about the axillae and loins, spreading over the abdomen, chest and back, almost never on the face, occasionally on the palms and soles. At first disappearing on pressure, it soon becomes petechial. The eruption may last for 2 to 3 days in mild cases or become markedly hemorrhagic with necrosis over points of pressure in severe cases. The rash fades with fall of fever Complications Bronchopneumonia, otitis media and parotitis azotemia, thrombosis of abdominal and peripheral blood vessels.

PATHOLOGY

Proliferative and thrombotic lesions in small blood vessels of the skin skeletal muscles, heart and central nervous system. In the grey matter of the brain typhus nodules with perivascular accumulations of mononuclear and polymorphonuclear cells. Rickettsiae may be seen in endothelial cells.

REACTIONS AND PHENOMENA

The rickettsiae may be isolated by cultivation in the chick-embryo

in guinea pigs febrile reaction occurs with no mortality passage in guinea pigs is accomplished by transfer of blood or brain from infected animals Indistinguishable from endemic (murine) typhus in cross immunity tests in guinea pigs but distinguishable from Rocky Mountain spotted fever and other rickettsial diseases in such tests Strains of *Rickettsia prowazeki* from various parts of the world are closely related as determined by specific complement fixation are distinguishable from other rickettsiae by agglutination, complement fixation and precipitin tests have a common antigenic factor with *Proteus* OX 19 and have a soluble antigen in yolk culture Immunity



543 The secondary lesion. The dermis and the deep part of the epidermis show an inflammatory infiltrate. Two dermal capillaries are obliterated.

prolonged but may not be complete in man. Killed vaccines produced from infected lice and from infected yolk sacs afford a high degree of protection against the disease. Hyperimmune antisera for therapeutic use have been produced in rabbits by injection with infected yolk-sac suspensions and in horses and donkeys with infected mouse-lung suspensions

DIAGNOSIS

Before the rash appears likely to be confused with endemic (murine) typhus, smallpox, relapsing fever malaria typhoid fever meningo-

coccic meningitis, measles and yellow fever. The eruption of Rocky Mountain spotted fever appears first on the wrists and ankles, and then spreads to trunk. Epidemic typhus can usually be differentiated from endemic typhus by specific complement fixation tests except in persons who have previously been vaccinated with killed rickettsial vaccines. In inoculated guinea pigs the endemic rickettsiae cause a scrotal reaction the epidemic rickettsiae do not. Louse-borne relapsing fever may exist in epidemic proportions together with typhus careful search for spirochetes in the blood serves to separate the two diseases

THERAPY

General supportive care except in the presence of edema, fluid intake should be regulated to produce a 24-hour urine output of 1500—2000 ml. The diet should be high in proteins, vitamins and calories to make up for the excessive destruction of protein. Chloral hydrate or paraldehyde may be used in the control of active delirium or extreme restlessness barbiturates should not be used and morphine should be used with caution. Digitalis and other cardiac drugs of no use unless unequivocal indications for their use are present. Sulfonamides have a deleterious effect on the course of typhus. Plasma, whole blood or isotonic albumin solution intravenously for azotemia or peripheral vascular failure Immune serum is valuable if used very early in the disease. Aureomycin or chloramphenicol given intravenously or orally will effect almost immediate improvement with convalescence beginning about the third day after treatment has been started. Initial dose is 60 mg/kg/body weight divided into three doses at hourly intervals, followed by 0.25 to 0.5 g every three hours until a few days after the temperature is normal.

RECENT ADVANCES

Epidemic typhus can be controlled by the following measures Isolation and delousing of all patients with typhus fever All attendants should be immunized with typhus vaccine and protected from lice by daily use of DDT powder Vaccination should consist of two subcutaneous injection of typhus vaccine, 1 ml each, at a seven-day interval Re immunization by injection of stimulating dose of 1 ml every six months Weekly use of DDT powder on underclothing inner surfaces of shirt and trousers and on hair of scalp

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BRILL'S DISEASE

DEFINITION

An acute recrudescence of epidemic typhus with fever generalized rash, duration of about 2 weeks milder than typhus fever and mortality nil

Synonyms are Recrudescent epidemic typhus American form of European typhus fever tabardillo

HISTORY

First published by NATHAN E. BRILL in the *Am J Med. Sci.*, 1910 a report of 221 cases observed in New York from 1896 to 1910 ANDERSON and GOLDBERG (1921) transmitted the infection to monkeys and demonstrated reciprocal cross-immunity with a strain of classic epidemic typhus ZINSSER (1934) concluded that it was recrudescence of epidemic typhus

EPIDEMIOLOGY

Immunologically identical with epidemic typhus It is European typhus brought to the United States by immigrants from the typhus

regions of South-eastern Europe. Of the more than 500 cases which occurred in Boston and New York between 1910 and 1933 more than ninety per cent. were in the foreign-born louse and contact infections could be excluded no vectors found.

AETIOLOGY AND PATHOGENESIS

Rickettsia prowazeki DA ROCHA LIMA (see epidemic typhus) Infection which was acquired in childhood remains quiescent until a recrudescence occurs many years later with symptoms milder but like those of epidemic typhus.

SYMPTOMATOLOGY

Prodromal symptoms for 3 to 4 days of malaise, loss of appetite nausea and slight headache onset sudden with vomiting severe headache, rapidly rising fever which attains its height in 2 to 3 days and then is continuous until terminating by crisis or rapid lysis after about 2 weeks. Rash on 5th to 7th day first on the back and abdomen, spreading rapidly to the thorax, arms and thighs, occasionally to the neck, forearms, legs and feet maculopapular erythematous fading somewhat with pressure lasts until the fever falls and then fades to dirty yellow stains. Pulse full and slow Recovery complete and rapid.

PATHOLOGY

See epidemic typhus.

REACTIONS AND PHENOMENA

Rising agglutinins for the *Proteus* OX 19 organisms starting from the 5th to the 8th day and reaching a peak during the third week. Complement fixing and agglutinating antibodies against the rickettsiae of epidemic typhus reach peak titer during the third week.

DIAGNOSIS

From epidemic typhus by history of childhood in regions where epidemic typhus occurs lack of infestation with lice from endemic (murine) typhus by complement fixation or agglutination tests against specific antigens from virus pneumonia by the appearance of the eruption.

THERAPY

Aureomycin or chloramphenicol or terramycin (see treatment of epidemic typhus) symptomatic therapy for headache and restlessness parenteral fluids for dehydration. Mortality negligible

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CHAPTER 28

EXANTHEMATA IN THE DENGUE GROUP

R. D. G. PH. SIMONS

Amsterdam

DEFINITION

Dengue is an infectious disease, often occurring epidemically, and caused by a filtrable virus transmitted chiefly by the mosquito *Aedes aegypti*, formerly called *Stegomyia fasciata*. Dermatologically, dengue is characterized especially by a morbilliform or scarlatiniform exanthema, sometimes even purpuric, coupled with fever, headache, muscle and joint pains, and swollen glands.

Dermatologists who are not at the same time general practitioners—which is not often the case in the tropics—rarely come across dengue, as they are not usually consulted for it. This is not to say, of course, that they need not be familiar with it.

The name "dengue" probably derives from the word "*dandy*" (or *denguero*) on account of the patient's stiff gait, caused by the pains in bones and muscles (cf. also *breakbone fever*, "*giraffe disease*," "*broken wing fever*," "*polka fever*" (Brazil)). The disease is also known by the name of "*[illegible] Red fever*," but this term is more frequently used for murine typhus, which in an incipient form may resemble dengue fever.

EPIDEMIOLOGY

Dengue is found nearly everywhere in the tropics and subtropics. In 1928 it was also observed epidemically in Greece and Egypt

Epidemics of dengue have occurred in different tropical and subtropical countries *i.e.* in regions infested by Aedes mosquitoes.

AETIOLOGY

ASHBURN and CRAIG in 1907 found a filtrable virus in the peripheral blood of dengue patients during the first days of fever. HOFFMANN, MERTENS and SNIJDERS injected volunteers in the Netherlands with dried serum of dengue patients from Indonesia. These volunteers contracted dengue after a ten-day incubation period.

BLANC, in a similar experiment, found an incubation period of three days.

MANOUSSAKIS found that the virus can be transmitted by inoculation of fresh blood, when the incubation time was about a week. In most cases, however, the virus is transmitted by *Aedes aegypti* (BANCROFT) and not, as used to be thought, by *Culex fatigans* (GRAHAM).

When the patient has been stung by the mosquito, one or two weeks must elapse before the disease breaks out. In colder climates—*i.e.* below 18° C—the mosquito is either absent or does not become infected.

Dengue may also be transmitted by other genera of mosquitoes, *e.g.* *Aed. albopictus* and *Aed. scutellaris* (MACKERRAS, 1946). *Aedes aegypti* is also the transmitter of the yellow fever virus. On epidemiological grounds some sort of relation is suspected to exist between the two diseases. It has been asserted that dengue never occurs simultaneously with yellow fever in one and the same country. Yellow fever is followed by lasting immunity, which is far from being always the case with dengue, and definitely not with forms of dengue originating from other countries. Thus, "*Java dengue*" does not make the patient immune against "*Sumatra dengue*" and vice versa, as was proved experimentally by SNIJDERS. During the war SABIN, in experiments with volunteers, showed that there exist at least three distinct immunological types of dengue virus, which produce cross-immunity for a short period only but complete immunity to the homologous virus during the entire period of observation (2–3 years).

These findings readily explain the empirically proved fact that it is possible to contract dengue several times in the tropics, which has led

to the incorrect notion that the disease does not leave the patient immune to further attacks

What is certain is that the dengue and the yellow fever viruses are not identical DINGER succeeded in infecting mice intracerebrally with the yellow fever virus (resulting in fatal encephalitis) but not with the dengue virus. (SABIN and SCHLESINGER recently succeeded in inoculating mice with an especially virulent strain of dengue virus from Hawaii.)

The possibility that dengue may give a certain protection against yellow fever should not be entirely rejected. SCHUFFNER, DINGER and SNIJDERS succeeded in immunizing rhesus monkeys against yellow fever by infecting them with dengue

SYMPTOMATOLOGY

After an *incubation period* of between four and fourteen days the temperature rises peracutely the fever being accompanied by violent headache localized particularly behind the eyes. Movements of the eyes are also painful. An *initial erythema* appears (frequently but not always) on the face sometimes in small, sometimes in large spots, occasionally itching, sometimes multiform, and in some cases even urticarial. The pulse, at first rapid becomes slow by the end of the first week The patient complains of pains in the muscles and joints. The *blood picture* shows leukopenia with relative lymphocytosis. The initial exanthema disappears after one day the fever after about three days. The patient then feels much better but two days afterwards there is *a second attack*, of slightly shorter duration. During this second attack—*i.e.* between the 2nd and 5th days after the onset of the disease—*the terminal morbilliform or scarlatiniform exanthema* breaks out, starting on the hands and feet and spreading fairly rapidly over the entire body

The—often severely itching—dengue exanthema is polymorphous, because it may also be urticarial, and, in some cases even appears similar to that of erysipelas *i.e.* when it does not spread over the whole body. In a few cases there is *purpura* resembling an exanthema peculiar to one of the rickettsioses. The exanthema is sometimes coupled with enanthema; in other cases there is epistaxis. In many cases the cervical

and inguinal lymph glands are swollen. After one or two days the exanthema disappears, leaving a slightly scaly skin.

Possible complications are, purpura of the skin and mucous mem-



544. Secondary rash of dengue fever
(*Snyders—Amsterdam*)

branes, sometimes acetonuria (JOYEUX), albuminuria, parotitis and orchitis (DE LANGEN, WEYRAUCH and GASS), affections of the heart and lungs (WAKIL and HILMI), neuritis (KAPLAN and LINDGREN), haematemesis (LAIGRET), haemorrhages and petechial exanthema

(HITTI and KHAIRALLA) and encephalitic phenomena (MELISSINOS). The lesions are less distinct on the dark skin than on the white skin. A small percentage of patients die of the disease (maximally 2 % (FEGHALI, Beyrout)) but as a rule recovery is spontaneous. A remarkable detail is that the disease is usually followed by a period of sleeplessness and mental depression. In popular parlance a dengue patient is "five days ill, and five weeks down in the mouth"

DIAGNOSIS

Dengue should be distinguished from toxicoderma in other febrile diseases, *e.g.*, quinine exanthema in malaria, or antipyrine exanthema in influenza. Measles shows the so-called "Koplik's spots". Scarlet fever is coupled with sore throat. Polyarthritis rheumatica with a salicyl exanthema is of longer duration. Yellow fever may resemble a grave form of dengue, the most important difference being jaundice, which never occurs in dengue. Although yellow fever, in a few cases does not set up jaundice it never happens that a yellow fever epidemic is unaccompanied by jaundice. Synonyms of dengue are in Indonesia, *five day fever*, *Van der Scheer's fever* and "*Palembangitis*". The same type of fever is also said to occur in other countries, its duration varying between three and ten days. In Panama, DEEKS described a "*six-day fever*" coupled with splenomegaly. *Colorado tick fever* is probably a type of the dengue-group. It has, however specific immunological characteristics, which have yet to be confirmed. A cutaneous rash (see pag. 91) is rarely seen.

In common with DINGER, DE LANGEN and SNIJDERS, most authors assume today that *Van der Scheer's five-day fever* and *Roger's seven-day fever* (or "*Japanese autumn fever*") are both dengue. In addition to yellow fever there is also in the Congo, *red fever* but this has now been definitely identified as murine typhus fever.

Rift valley fever, *East African hepatitis* and *Bwamba fever* in Uganda too are not forms of dengue although there is a clinical resemblance.

Mud fever caused by Leptospira grippo-typhosa can hardly be distinguished from dengue.

The *three-day fever* or *pappataci fever* also called *sandfly* or *phlebotomus fever* is better known. It is found chiefly around the Mediterranean, but also in India, China, Africa and South America. This disease is

transmitted by *Phlebotomus pappatasi* i.e the sandfly (not to be confused with the sand flea or sika, described in volume II)

Pappatasi fever closely resembles dengue but the second attack is omitted. It also begins with a red face and strongly swollen conjunctivae, headache behind the eyes and a general feeling of malaise. The patient may feel seriously ill and be apathetic. Nose bleeding is frequent.

THERAPY

The therapy of all these dengue fevers is purely symptomatic. In addition to antipyretics sedatives are administered. Sulphonamides do not act therapeutically and must be advised against, as they are liable to aggravate the concomitant leukopenia. LE GAC recommends lumbar puncture in cases with severe headache, stiff neck lumbago and bradycardia.

Experiments with wholesale prophylactic vaccination in the American army in the Pacific yielded no favourable results.

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CHAPTER 29

BARTONELLOSIS

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DEFINITION

Bartonellosis is a non-contagious infectious disease transmitted by the phlebotomus, including two strikingly different phases or types, (1) *verruga peruana* presenting a characteristic eruption, followed nearly always by complete recovery and (2) *Oroya fever* characterized by severe constitutional disturbances, including anemia of the pernicious type. Synonym *Carrion's disease*

HISTORY

Little is known about the early history of the disease which probably existed in Peru for centuries and is said to have been the cause of death of one quarter of the army of Pizzaro, the Spanish Conqueror Little accurate knowledge was known about the disease previous to 1870 when a railroad was built over the Andes from Lima to Oroya. This caused a severe epidemic during which it is said that 7 000 work men died. They were mainly Chileans who were not immune to the disease Of the 100 British and American engineers who built the railroad, all contracted the disease and one half of them died of it. Opinions differed regarding the nature of the new disease. Some considered it a modified form of malaria, while others thought it was a severe type of verruga peruana, an opinion which was later substantiated. The opinion that Oroya fever and verruga peruana were different types of the same disease was finally settled in the minds of

Peruvian physicians by the experience of a medical student, DANIEL A. CARRION. In 1885 he allowed himself to be inoculated on the arm from a patient suffering from verruga. Unfortunately he contracted the severe Oroya fever and died 39 days later. In 1913 TOWNSEND reported phlebotomus to be the transmitter of the disease. The first good description of the disease was published in 1939 by PATINO and CAMARGO when bartonellosis occurred in Colombia because of the war with Peru in 1933.



545. Profuse eruption on the extensor aspect of the extremities preceded by fever, muscle pains, vomiting and diarrhoea in a man, aged 42. The duration of the eruption was fifty days. Many lesions are in the process of evolution, showing scaling and crusting.

EPIDEMIOLOGY

In Peru the disease is confined to certain areas on the western slope of the Andes. It occurs in narrow canyons at altitudes approximately 2,500 to 9,000 feet. It does not occur in the coastal or high mountainous region. There was a probable epidemic of Bartonellosis in Colom-

bia in 1936 where the mortality reached 40 per cent. with 1800 deaths The disease has also been recently seen in Ecuador and Guatemala.

Bartonellosis occurs in both sexes at all ages and in all races. The disease runs a mild course in children up to about ten years of age but becomes severe in adolescence and adult life. Most of the inhabitants of the infected areas have acquired a permanent immunity due to having had a mild attack in childhood Human beings with active lesions constitute one reservoir of infection. It is also possible that persons with no outward signs of the disease may act in the same way All non-immune visitors to endemic areas are liable to be infected if they spend one or more nights without taking precautions against the bites of the phlebotomi.

AETIOLOGY

The causative organism of the disease was discovered in 1906 by A BARTON and was named *Bartonella Bacilliformis* by STRONG The organism is found in the red blood cells as rod-shaped or round bodies in preparations stained by GIEMSA's method. They occur singly in pairs or in end to end chains The number of organisms in the red cells vary from one to ten or more. They not only occur in the peripheral blood but also in many tissues, including the lymph nodes, liver spleen, intestines and cutaneous lesions. Opinions differ as to the proper classification of the organism. The present tendency is to classify them with the Rickettsiae.

It is generally thought that the first pure culture on a semi-solid nutrient medium was obtained by NOGUCHI and BATTISTINI in 1926 at the Rockefeller Institute in New York The successful cultivation proved through animal inoculations that verruga peruana and Oroya fever were different phases of the same disease. NOGUCHI reproduced verruga in monkeys from the blood of an Oroya fever patient. MAYER and KIKUTH reproduced Oroya fever in monkeys from human verruga lesions.

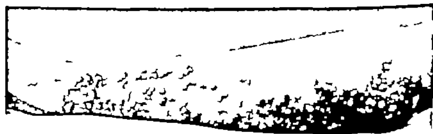
Experimental infections have usually been obtained by the inoculation of verrugous material in the skin, less often from cultures and almost never from blood, even when swarming with Bartonellae Many animals in Peru apparently suffer spontaneously from the eruptive type of verruga That at least is the general opinion. The fact that

various animals can be artificially inoculated is however no proof that they suffer spontaneously from the disease. JADASSOHN and SEIFFERT in 1910 were the first to transfer the disease to animals (monkeys). Other animals including the dog, sheep, goat, and rabbit have also been successfully inoculated. Among human inoculations, the experience of CARRION has already been mentioned. On the other hand, a Peruvian physician was accidentally inoculated by the blood of an Oroya fever patient while giving a transfusion. Fortunately he developed the harmless type of verruga and was well at the end of ten months.

The vector of the disease was conclusively proved by TOWNSEND in 1912–14 to be a species of phlebotomus which he called "*Phlebotomus verrucarum*." SHANNON later added two more species of sandflies as vectors of the disease. In 1930, after a careful botanical study in the verrugous regions, MALDONADO found certain lactescent plants to be solely characteristic of these areas. He suggested that they might play a role as a virus and as food for the vector. In 1935 MACKEHENIE and CORONADO obtained cultures under aseptic precautions from these plants showing the characteristics of Bartonella.

SYMPTOMATOLOGY

According to HERCELLES, hemorrhage and thrombosis are constantly present in the Oroya type of the disease. Bartonellae were cultivated



546. M[illegible] eruption with scaling and a few blood crusts.

from most of the tissues, notably the kidneys, spleen and bone medulla. PEDRO WEISS speaks of two types of the disease: *hematic* and *histoid*.

The former type is characterized by the presence of Bartonellae in the circulating blood, while the latter type is limited to the reticulo-endothelial system. He considers the formation of verruga lesions to be an allergic reaction to the virus

Between the two forms of Bartonellosis *(Oroya fever* and *verruga peruana)* there are innumerable gradations. Oroya fever is the malignant type of the disease with an *incubation period* of probably 15-40 days. In CARRION's experiment it was 21 days It is accompanied by chills and fever most often of the remittent type. A profound



547 V riation in size of lesions and tendency for older ones to be pedunculated.

anemia is characteristic and often extremely rapid. The red blood cells may decrease to 1 000,000 in three to four days, though usually this requires one to two weeks. The type of the disease is a combination of pernicious anemia and leukemia In severe cases all the bizarre forms of pernicious anemia are seen. The leukocytes increase, eosinophils disappear and myelocytes and myeloblasts may appear There are also large numbers of Bartonellae

The *incubation period* of verruga peruana, the benign type of the disease is probably the same as that of Oroya fever It is followed by (1) a *stage of invasion* and (2) an *eruptive stage* The invasive stage begins

with constitutional symptoms, including a mild fever usually of intermittent or tertian type, simple anemia, gastro-intestinal symptoms and more or less severe pain in the muscles and joints. The blood may also show Bartonellae but in much smaller numbers than in the Oroya fever type. The invasive stage lasts three to four months, when the constitutional symptoms disappear and the patient is on the road to recovery. The cutaneous lesions of the eruptive stage are unlike those of any other disease. Some of the lesions resemble senile angiomas or pyogenic granulomas, while others suggest a generalized sarcomatosis.

The eruption consists of two types of lesions, the so-called *miliary*



548 Profuse miliary eruption of the genitals, an unusual location.

or cutaneous type and the *nodular or subcutaneous type*. The miliary type occurs most profusely on the extensor aspect of the extremities and to a less extent on the face and neck. The palms and soles are usually spared and the genitals are only occasionally affected. The lesions begin as tiny papules which are hard at first but gradually soften after they have attained their maximum size, that of a split pea. Most of the lesions are discrete and of varying size, owing to their appearance in crops. Some of them disappear before attaining the maximum size. All lesions are sessile, hemispherical or rounded at first but some become pedunculated eventually. The overlying skin is at first soft

but later becomes wrinkled and may show the presence of blackish (hemorrhagic) crusts The color of the lesions is characteristic, all showing some shade of red. Itching is not a feature. The eruption lasts



549 A large nodule appeared over the first metacarpal bone of three months duration, not preceded by any constitutional symptoms, in girl, aged 10 months. The nod le was hemispherical, hard nd painless and co ered by normal skin freely movable over it. There were also a few miliary lesions on the face and two on the forearm.



550. Area ne r pedicle of mature miliary lesion, under medium high power showing irregular epidermis and a few dilated capillaries, several of which contain pigment and red cells. Deeper portion shows hemorrhage and pigment among cells of the infiltration

from four to six months or more and disappears without leaving any permanent trace.

The nodular type of the eruption appears in the subcutaneous tissue



551 Section of early miliary lesion in upper corium almost entirely encircled by acanthotic rete under low power. Shows proliferation of capillaries, many of which are dilated



552. Border [illegible] nodular d retrogressing lesion under low power showing band of sparsely [illegible] d corium separating epidermis and deeper infiltration. Strands of thickened [illegible] found in closely packed lymphoid cells. Blood vessels are [illegible] ished. Hemorrhage and pigment are absent

where it can often be felt before it is visible. This type of the disease occurs most often on the extensor aspect of the extremities. A rare type of the nodular form may be as large as a hen's egg or even a small apple. When traumatized, it may bleed profusely and even cause death from hemorrhage. The mucous membranes as well as the skin may be the sites of the miliary type of eruption, including those of the conjunctiva, nose, throat and gastro-intestinal tract. The mucous membranes are not affected by the nodular type.

The diagnosis of the Oroya fever type can only be made with certainty by demonstrating the presence of the Bartonellae. On the other hand, the diagnosis of even a moderate eruption of verruga can usually be made from its characteristic appearance.

THERAPY AND PROPHYLAXIS

There is probably no specific treatment for the disease according to the opinions of the physicians of Peru. Prophylaxis is all important and consists in remaining away from endemic regions after nightfall, as the sandflies which carry the disease are night-flying insects. According to TOWNSEND, no one has ever contracted the disease without having spent one or more nights in the endemic regions. During World War II six cases of Bartonellosis were reported in the United States Army and Marine Corps. HODGSON advises blood transfusions in combination with penicillin therapy. MACCHIAVELLO states having seen good results of autohemotherapy with the sediment of 10 ml of citrate blood twice weekly.

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CHAPTER 30

VARIOLA[1] (Smallpox)

J. E. DINGER

Leyden

DEFINITION

Variola is a cosmopolitan, epidemic, acute exanthematic infectious disease to which man is naturally highly susceptible. Its geographic spread accordingly depends exclusively on prevailing hygienic conditions such as universal vaccination, quarantine regulations, early diagnosis and isolation of cases and contacts.

Smallpox is the same as variola. "*milk pox*" or "*kaffir pox*" is variola minor or alastrim. "*chicken pox*" is varicella. "*monkey pox*" is pyosis Mansoni. *Amboyna pox* is a term formerly used to denote the papules in yaws. "*Spanish pox*"—or just "pox" is an English term for secondary syphilis. Rickettsial pox is a rickettsial disease.

Vaccinia is variola inoculata or *cow pox* which appears after vaccination. It resembles smallpox [illegible] the lesions are bullous or pustulous, in contrast to *paravaccinia* (a telangiectatic papules which appear at the place of vaccination. The papule is often haemorrhagic. It is an open question whether paravaccinia is caused by the variola virus or by the strongyloplasma paravaccinia of Lipschütz. The term paravaccinia also refers to what is commonly called "*milker's nodes*" [illegible] vaccinia or paravaccinia on the hands of milkers sometimes followed by a papulous exanthema of the entire arm. They should not be confused with "milker's [illegible] of milker's [illegible] or granuloma telangiectaticum.

When vaccinia spreads over eczema the result is called *eczema vaccinatum*.

The *amaas* of Central Africa is said to be not a special form of smallpox or kaffir pox, notwithstanding the name of *malignant* [illegible] given by [illegible] this disease. It has only a few hours (up to one day) incubation period. The

[1] The term is in the singular. The plural would be variolae majora or variolae verae.

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are found in the cells of the pock and of the infected cornea. The actual virus is supposed to be PASCHEN's elementary bodies which can be demonstrated both in the preparations of infected allantoic membranes and in the contents of variola pustules.

Manner of transmission The variola virus is present on the skin and



554 Umbilicated smallpox, some of which are confluent.

mucous membranes of the smallpox patient, from the prodromal stage until the crusts fall off Transmission is both by direct contact and airborne the probable porte d entrée being the respiratory organs.

Transmission from a distance may be either airborne via objects, or—probably also—through flies.



555 Smallpox with acantholysis under the garter



556 Smallp… Not… mbilication and localisation along the tendons.

EPIDEMIOLOGY

Variola, which should really be classed with the ubiquitous diseases, has, by now been practically restricted to the tropics and sub-tropics A fact to be kept in mind is that, in a community where only 50 % of the population is, as yet, immune, an epidemic among the remaining half is still quite possible.

Whereas the importation of virulent smallpox into a non-vaccin



557 Variola minor or alastrim. The second rise of fever common in variola, fails to appear

(Pons-Nabold)

ated community is generally followed by a serious pandemic, It is said of alastrim that the disease may "smoulder" among certain sections of the population. Sporadic cases of alastrim may then be found from time to time but the disease does not assume an epidemic character to the same extent as smallpox does. Transition from the

benign to the malignant form, has not, so far, been ascertained. One great danger is the fact that, during an epidemic, healthy persons are inclined to flee from the smallpox infected area. If they do so during the incubation period they may transmit smallpox to some other place.

SYMPTOMATOLOGY

After an *incubation period* of 8–14 (usually 12) days, the *prodromal stage* begins with cold shivers and hyperpyrexia, which may reach 41 °C (± 106 °F), severe headache and violent pain in the lumbar region and limbs, sometimes sickness and vomiting and often coupled—especially in children—with pain in the epigastrium. The tongue is coated, there is foetor ex ore, the skin is dry, sweating does not start till later on. In a percentage of cases there is an *initial rash* which may resemble either scarlatina, measles, erysipelas or urticaria. This rash may be haemorrhagic.

The *exanthema* (at first macular, afterwards papular) generally starts on the 3rd day in milder cases, and sometimes later. In another 2–3 days the exanthema passes into the *vesicular stage*, involving especially the uncovered skin up to the hair-covered part of the head. The completely developed smallpox is round, umbilicated, and surrounded by erythema. The contents are clear. After some days the contents become purulent; by the 9th–10th day the pustule thus formed has grown to about 11–12 mm.

When the exanthema breaks out in *one* eruption (this in contrast to chicken pox) the patient feels much better; the temperature usually falls to normal, rising again subsequently during the *suppurative stage* as a result of secondary infection of the pustules with strepto- and or staphylo-cocci. The pox then dry up, and during the 12th–13th day the crusts so formed begin to fall off, leaving reddish-brown spots which later turn into scars (*cf.* histology). The *crust stage* is generally coupled with considerable irritation of the skin.

Smallpox may be divided into *variola vera* and *variola haemorrhagica* according to the form of the exanthema.

In variola vera the pox may either remain disseminated (*variola vera discreta*) or run into one another (*variola vera confluens*). Abortive cases (*varioloid*) may sometimes show no exanthema (*varioloid sine exanthemate*).

In variola haemorrhagica we distinguish between *purpura variolosa*

and *variola haemorrhagica pustulosa* The former appears during the initial stage on the 2nd or 3rd day after the onset of fever extensive haemorrhages are seen, with violet to blue black discoloration, sometimes coupled with haemorrhage from the mouth, ears and eyes, and with haematuria. The prognosis is bad death sometimes super



558 Variola minor The number of pox is of no significance for the diagnosis. *(Piers-Nabrold)*

venes after a few hours, but, at the latest, on the 6th day after the first haemorrhagic symptoms.

Variola haemorrhagica pustulosa ("black smallpox") appears during the vesicular stage bleeding is limited to the tissues immediately beneath and around the blisters In some cases large blisters are found filled with blood The prognosis, here too is serious but not as bad

as in purpura variolosa. A bad sign is the appearance of fresh pox on the slightest pressure (*cf* NIKOLSKY's *phenomenon* in pemphigus vulgaris)

The patient's general condition includes albuminuria and, in the beginning leukopenia followed by leukocytosis with toxic granules during the suppurative stage. In pregnant women abortus generally follows. Other complications are bronchitis pneumonia, laryngitis,



559 Pigmented spots following smallpox. *(Piers–Nairobi)*

corneal ulcer hypopyon and panophthalmia furuncles carbuncles, abscesses phlegmonas erysipelas and otitis media. Of lesser frequency are pleuritis and empyema Corneal turbidity blindness and alopecia may result from affection of the eyes and scalp

HISTOLOGY

According to BRAS the uncomplicated pock is, mainly an intra epidermal lesion Histologically the first dermal changes appear in the sub-papillary anastomoses network, after which the pustule is formed in the corresponding area of the epidermis Cicatrization is usually the result of secondary infection, except as regards the face

where the destruction of the greatly developed sebaceous glands leaves a shrunken scar after recovery producing the type of skin commonly called "pock marked"



560. *Punctate leukoderma following smallpox.*
(Pers-Narold)

DIAGNOSIS

The clinical diagnosis of typical cases is easy during an epidemic. Primary cases may present difficulties, especially when taking a mild course as, for instance in vaccinated persons arriving from a small pox infected district And it is precisely in such cases that early diagnosis is of such supreme importance from the epidemiological angle.

In the prodromal stage the disease may be confused with scarlet fever, measles, rubella, typhus, influenza, or lumbago. After the eruption, measles, rubella, erythema exsudativum multiforme bullosum, with general feelings of illness and involvement of the mucosae, and more particularly alastrim, vaccinia generalisata and varicella, fall under the differential diagnostic. Measles and rubella are hardly ever either bullous or pustular and multiform erythema is urticarial. Herpes iris in erythema multiforme should not be confused with (umbilicated) smallpox.

Alastrim ("amaas", kaffir pox, white pox") is a mitigated variola: the eruptions may be equally widespread, but the general morbid phenomena are far less serious, while the mortality is nil.

Alastrim occurs especially in tropical and subtropical regions, but larger or smaller epidemics have appeared also in Europe, Britain, Switzerland. The virus, if not identical with, is in any case closely akin to that of variola, and vaccination gives protection against both diseases. Alastrim is now generally regarded as a mild form of smallpox. Practical considerations compel one to extreme caution in diagnosing alastrim: in primary cases it is advisable to take all precautionary measures prescribed for smallpox. *It should also be remembered that "mild smallpox" (varioloid) is quite as dangerous epidemiologically as variola vera.*

The most important differential diagnosis is that between variola and varicella—on the one hand for the protection of the community, and on the other hand in the interest of the patient, who might be wrongly admitted to a smallpox ward. SIEGENBEEK VAN HEUKELOM rightly stresses that, *during a smallpox epidemic, a ward should be set aside for not yet definitely diagnosed cases.*

In this differential diagnosis the course and distribution of the exanthema is an important factor. The smallpox exanthema generally starts on the face, especially on the forehead and lips, and on the hands and wrist, spreading later to the trunk and the arms, and finally to the lower extremities. In a developed exanthema the dissemination is densest on the face, hands and arms; more so on the lower than on the upper arm; more on the feet and lower legs than on the thighs; more on the extensor side of the extremities than on the flexor side; more on the back than on the front part of the trunk, and, here, more

on the chest than on the abdomen. Predilection places are, the exposed parts of the skin, particularly those spots which are, or have been, subjected to some form of irritation, such as scratches or burns, and where the edge of a shirt-band or collar sock-suspenders, shoes, etc. rub against the skin and further in those places where the skin lies close to the bone. Often the lesions are found along the extensors. Parts that are usually unaffected are, the palms of the hands, the armpits and groins the abdomen, the popliteal regions the crook of



561 Variol form syphilis.

(Fasal San Francisco)

the arm and the occipital triangle of the neck. In widespread eruptions on the face and shoulders the lesions may appear as it were, attracted by the sterno-cleido-mastoidus trapezius and collar bone, leaving a free triangle in between. According to SITGENBEEK VAN HEUKELOM the eruption is invariably bilateral, *any unilateral eruption casting doubt on the diagnosis*

Apart from the skin, the mucous membranes of the mouth, tongue, palate and larynx may also be affected by smallpox.

In *varicella* the exanthema does not have this characteristic distribution, it being localized for preference on the trunk. The varicella,

moreover are very often in different stages of development during the vesicular stage one may find some belated papules coming up which is rare in variola. The vesicles are not always umbilicated they usually lack a hyperaemic zone or inflammatory focus and the vesiculation of the papules follows more quickly. Further differences are that, in varicella, the eruption appears as soon as the fever starts (in variola on the 3rd day or even later), and that the fever persists after the appearance of the eruption.

During an epidemic of smallpox, *vaccinia generalisata* may put *difficulties in the way of the differential diagnosis. In such cases the* laboratory may render signal service in aiding the anamnesis and clarifying the clinical syndrome (see below)

TESTS

Outside epidemiological observation, and particularly in mild cases the only reliable diagnosis is the aetiological one. It is determined by demonstrating the presence of the variola virus in the lesions. There are several methods to effect this

(a) by PAUL'S *test* on the rabbit's cornea, the acidophile inclusion bodies of GUARNIERI are demonstrated in the cytoplasm. The diagnosis can only be determined after 72 hours and in addition this test turns out negative in about 50 % of cases of smallpox

(b) *inoculation of growing chick embryo* with the content of vesicles, or with suspensions of crustae gives practical certainty as to the diagnosis after 48–72 hours on the basis of the aspect of the resulting lesions. In contrast to PAUL'S test this method also lends itself to the differential diagnosis between smallpox and vaccinia generalisata. In case of doubt one may further differentiate between the variola and the vaccinia virus by additional transfers to chickens embryos and the skin of rabbits. The varicella virus does not grow on hatched eggs.

(c) The diagnosis may be regarded with satisfactory certainty as either positive or negative within 24 hours, with the aid of the *complement fixation* test first described by PARKER and MUCKENFUSS and performed with hyper immune rabbit's serum as antibody and the content of suspected vesicles or a crustal suspension as antigen.

(d) With the same materials one may perform a *flocculation test* according to GORDON, CRAIGIE and FULLOCK.

(e) The possibility of an early diagnosis is mentioned in the recent literature (MEGAY KAISER), by provoking an allergic dermal reaction in suitable testees with the aid of the content of suspected vesicles in which the virus has been destroyed by heating (*cuti-reaction according to* TIÈCHE)

(f) Finally a test which can be made without the aid of the labor atory and which may give considerable support to an early diagnosis, *i.e.* microscopic demonstration of PASCHEN's inclusion bodies in a slide preparation of the content of the variolar vesicles. This is done as follows. Some of the contents scraped from the bottom of a vesicle are smeared on to a slide and dried in the air The slide is then carefully placed—vertical—into water or into a physiological saline solution for 3–10 minutes and put out to dry again vertical, after which it is fixed in methyl alcohol (5 mins) and rinsed in running water for 2 minutes. It may now be stained according to VAN ROOYEN and ILLINGWORTH or better still, according to GIEMSA (1 drop Giemsa to 1 ml neutral aq dest. stain for 1 hour renew solution every 20 mins). PASCHEN's elementary bodies colour metachromically as chromatin they are granules of about 200–250 mμ diameter partly disseminated and partly in clumps. In varicella too, elementary bodies are found they however are smaller and fewer in number and not clumped but isolated.

PROGNOSIS

The prognosis is sometimes difficult and depends on the clinical findings. The *case fatality rate* among the non-vaccinated is high that of purpura variolosa is 100 %. In variola vera confluens it is higher than in variola discreta. Among a partially immunized population variola presents a widely varied picture (SIEGENBEEK VAN HEUKELOM) with a great many mild and ambulant cases.

As regards the age-factor among the non-vaccinated the case fatality rate is highest in children under 5 and lowest between 11 and 15 years of age

Variola in pregnant women usually leads to abortion the uterine infection starts from the third month of pregnancy and the foetus may be born at any stage of the eruption. Recovery in utero is possible cases are known of children born with variola scars.

SIEGENBEEK VAN HEUKELOM has described a case of a pregnant woman with smallpox who was delivered at nine months of a child who had remained free from smallpox.

THERAPY

The therapy—so far as infection with the variola virus is concerned—is entirely palliative, but modern antibiotics and sulfa drugs are extremely useful in countering secondary purulence, and, therewith, in preventing a good many complications. They accordingly have a considerable influence on the prognosis as well as on the possibility of mitigating cicatrization. In purpura variolosa therapy of any kind is completely impotent.

PROPHYLAXIS

The prophylaxis against variola consists in active immunization of the population by means of vaccination. Since the patient is the carrier of the virus and smallpox is spread by contact, vaccination is not only important for the individual but it also stops the disease from spreading. It has been shown that, even in tropical countries, vaccination once every 10 years is sufficient to prevent smallpox epidemics. In the case of threatened infection, re-vaccination should be done at shorter notice. For testing individual immunity COLLIER attaches great value to the haemagglutination-inhibition titre of the serum.

A *vaccination certificate* is internationally valid provided that it states the result of the vaccination, *i.e.* immediate reaction, accelerated reaction, or primary reaction. Whenever there is no reaction, either the vaccine was at fault or the inoculation was inadequate for some other reason; the person must then be vaccinated once more. The value of an early reaction as proof of successful vaccination is today being doubted by many: it is, in fact, an allergic reaction which may also be provoked with dead virus in persons who have been vaccinated before. In the British army the only criterion now adhered to is the appearance of pox. In their absence vaccination is repeated (NIVEN).

In different European countries *encephalitis postvaccinalis* has become a serious obstacle to vaccination. Since this complication is extremely rare in primarily inoculated infants, as well as in re-vaccinated

persons of any age, the best prophylaxis, both against smallpox and against encephalitis postvaccinalis, is vaccination of all children during the first year of life.

Encephalitis postvaccinalis has not (yet) been ascertained with absolute certainty in tropical countries. Two cases of encephalitis *after* vaccination have been described in Indonesia (SIM, KOPERBERG) of these, it is not certain whether they were "post" or "propter". One certain case of encephalitis postvaccinalis has been described in



56. Third Hand Vaccinia. A soldier who was vaccinated on his thigh infected girl on her thigh. She again infected another friend on his face.

(Gratfeld–Berger [illegible] Zeeman)

Indonesia: this, however, concerned a Dutch soldier inoculated on a Dutch troopship with vaccine obtained from the Netherlands (BRAS and VERHAART).

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CHAPTER 31

LYMPHOPATHIA VENEREA

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DEFINITION

Lymphopathia venerea is a tropical venereal disease chiefly characterized by either unilateral or bilateral often suppurative inguinal lymphadenitis and periadenitis. A specific primary lesion is seldom found, the bubo therefore, being a "bubon d'emblée" The iliac lymphatics are practically always involved. Frei's test (described below) is specific. The disease is more often diagnosed in men than in women. The term lymphopathia venerea was introduced by Wolf and Sulzberger because the notion "lymphogranuloma inguinale" tended to be confused with "granuloma venereum" The new term cuts out the word "granuloma" which was the cause of the confusion. Other names for the disease are, Nicolas Favre Durand's disease poradenitis poradenolymphitis (Ravaut), and climatic bubo (Scheube) Another benign, lymphogranulomatosis is Schaumann Boeck's disease malign lymphogranulomatosis is better known by the name of Hodgkin's disease

EPIDEMIOLOGY

Lymphopathia venerea occurs almost exclusively in the tropics although it may also be found—perhaps even autochthonous—in some non tropical regions. Imported cases are occasionally met with in European seaports. The disease was imported by sailors into Finland, where an epidemic broke out during the years between 1925 and 1938

It was especially at that time that opportunities occurred to study the course of the disease also in women.

HISTORY

The disease, which had already been known for a long time under various names, *e.g. althaema strumae paenas* and *climatic bubo*, was described in detail in 1913 by NICOLAS, FAVRE and DURAND in France, under the name of "*lymphogranulomatose inguinale aigue cutanée d'origine génitale*"—for which reason it has since been named after these authors. In 1922 PHYLACTOS stated that the disease was not identical with either tuberculosis, HODGKIN's disease, plague, syphilis or ulcus molle but that it was a disease *sui generis*.

In 1925 FREI described the reaction which was later called after him as diagnostic of the affection.

In 1930 HELLERSTRÖM and WASSÉN succeeded in provoking meningoencephalitis in the monkey (macacus rhesus) by inoculation with the virus.

In 1934 the virus was cultivated by TAMURA and in 1937 NAUCK and MALAMOS obtained the first embryonic culture.

After NICOLAS (1938) had described virus bodies, discovered as early as 1927 by GAY and PRIETO, as being the causative agents, these micro-organisms were termed *pararickettsiae Miyagawae* by LEVADITI in 1943.

In 1941 SONCK described the phenomenon of photo-sensitivity in lymphopathia venerea.

AETIOLOGY

The disease is caused by a filtrable virus (LEVADITI 1932), small cytoplasmic double granules (FAVRE), or the intra- and extra-cellular bodies of GAY and PRIETO (1927), which are akin to Rickettsia (MIYAGAWA 1935) and now called *pararickettsia Miyagawae* (LEVADITI 1943). The pararickettsiae are found in every specific affection with the disease, chiefly in the later stages. SABIN and ARING found the virus in the spinal fluid.

Intracerebral injections in monkeys, rats, mice, guinea pigs and dogs set up lethal meningo-encephalitis. In guinea pigs and monkeys, injection of the virus into a lymphatic gland may cause a bubo.

Staining may be done either by the GIEMSA method (1–14 hours) or by that of MACHIAVELLO. In the latter case a basic fuchsin solution is used for 4 minutes, after which the stain is washed with water. After this, ½ % citric acid is added and washed off again immediately followed by a 1 % methylene blue solution (20 seconds) and washed again. The paranickettsiae will then be stained red in a blue-coloured milieu.

SYMPTOMATOLOGY

After an *incubation period* of between 3 and 25 days (according to SÉZARY as long as 3 months in some cases), a swelling of the lymphatic gland appears, fairly acutely in the groin above Poupart's ligament. The swelling may increase day by day and is coupled with *periadenitis*. This *adenitis* is unilateral in two-thirds of the number of cases, either on the right or on the left side and bilateral in about a third, when however it usually starts a little earlier in one groin than in the other (SIMONS). Owing to the periadenitis (called "*adénite violette*" by FAVRE) the lymphatic glands adhere together as well as to the skin, causing the latter to turn a reddish-purple colour. The skin feels hot to the touch. In about one-third of cases there is no periadenitis. After about a week or longer the affected lymph gland begins to soften. This softening process however is *not* "*en bloc*" but *multilocular*" so that the fluctuation cannot always be felt, and definitely not always in the beginning. In this case the *presence of suppuration may be ascertained* by an exploratory puncture at the spot where the hard node feels somewhat softer to the touch.

FREI found distinct suppuration in only 18 of his cases but in view of the above it should be clear that partial softening (and this is precisely the characteristic feature of this disease) *is present in almost* 75 of cases (SIMONS). This softening may be the cause of a number of fistulas which secrete thick cheesy pus, and which leave ugly scars on closing up. The pus contains some polymorphonuclear leukocytes, and many mast cells as well as the so-called "*gamma bodies*" which, however according to PHYLACTOS are mere "*débris protéiques*". The disease is nearly always coupled with slight fever.

Thus far as regards the classic picture which is found far more often in men than in women. The probable reason for this is that the regional

lymphatics of the posterior vaginal wall—the most likely location of the primary affection—lie perirectally in the pelvis. Nevertheless inguinal lymphadenitis does occur also in women; in many cases however there is only marked swelling of the labia majora and minora, and *periproctitis* which may lead to fistulae or strictura recti.

Adenitis in lymphopathia venerea may sometimes appear in other places besides the groin. It has been found, by HELLERSTRÖM and CURTH, in the armpit and in the neck. COUTTS described cheilitis and glossitis following oral coitus. According to FERRARI and CAMINOPETROS there is also a latent form of lymphopathia venerea: in women this is almost the rule, in men, the exception—at any rate if one is to call the disease "latent" when it escapes discovery owing to the slightness of the symptoms or inadequate examination.

There is no generalized swelling of the lymphatics in this disease. If there is, then the patient most probably has also secondary syphilis or another lymphadenopathy (bubonic plague!).[1] SONCK has described a case of "*Senkungs Abszess*" in the scrotum in lymphopathia venerea.

The patient with NICOLAS FAVRE's disease is liable to yet other morbid phenomena, the most important being the *iliac lymphadenitis*. In this, palpation of the diseased side of the abdomen reveals—at any rate in 75 % of cases—small hard nodes. In some cases one may even find an infiltrate the size of a child's head, and called "*placard inflammatoire*"; it is hardly, if at all, painful; nevertheless one wonders how a patient with an infiltrate that size can go on feeling practically fit and carry on with his work. This "placard inflammatoire" is found in about half the cases. In about 25 % of cases one only finds a few loose, hard iliac glands, which should be differentiated from scybala by giving a clysma. *Iliac lymphatics do not suppurate*; the phenomenon, however, is highly important and of considerable diagnostic value (SIMONS) for it appears at an early stage and disappears spontaneously when the patient has recovered, although, in rare cases, it may persist for a few weeks longer. The reason why to me

[1] A bubo below Poupart's ligament may be found in many inhabitants of the tropics. This femoral bubo, however, is usually a result of an infection of the foot, e.g., in "bathroom eczema". Although not, as a rule, coupled with suppuration it appears that, in rare cases, this femoral bubo does soften "en bloc". See also filariasis and the chapter on adenitis in the tropics.

iliac lymphadenitis is perhaps more valuable than Frei's reaction (described below) is that the latter (a) does not appear at the onset of the disease (b) may remain positive for years (which may lead to wrong conclusions, especially—and this is far from rare—when the patient gets another bubo) and (c) because the iliac lymphadenitis is easily found without special aids It seems that some cases may be

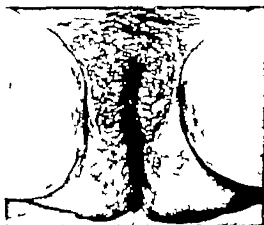


563 Relapse of lymphopathia venerea in old scar

f ll wed by peritonitis appendicitis and salpingitis but this to my mind, is of theoretical rather than practical interest.

Perirectal lymphadenitis as such, is found very infrequently it is, however of considerable importance in that it may lead—especially in women—to periproctitis (in some cases fistulous) and stricture of the rectum. It was a long time before this narrowing process—which may also pass on to the vulva—was recognized as a concomitant phenomenon of lymphopathia venerea The affection was described in 1848 by Huguier under the name of "*esthiomène*" or "*dartre*

rougeante de la région vulvo-anale" It is also known by the name of *elephantiasis genito-rectalis* and even under that of *syphilôme ano-rectale* —a term more appropriate to tertiary syphilitic changes in the rectum, with which, in fact, it was formerly confused. The name by which it is now most generally known is the *genito-ano-rectal syndrome of* JERSILD SONCK also found some cases of this affection in children. (In a number of cases of induratio penis plastica Frei s reaction was positive (cited from SONCK) In some 30% of cases of NICOLAS FAVRE s disease the *spleen* is also *enlarged* It may sometimes be felt as far as three fingers width under the abdomino-thoracic arch (SIMONS) It is, of



564 Elephantiasis genito-rectalis or "dartre rougeante de la région ul anale *(Lake-Berka)*

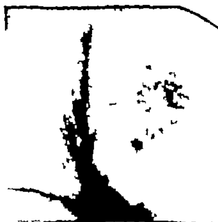
course pos ible—and probably not even exceptional—that the patient has a malaria spleen" but the present writer found in a hospital for native soldiers all of whom hailed from the same region, 5 splenomegaly in patients not admitted for NICOLAS FAVRE s disease and as much as 30 in patients with lymphopathia venerea

When no malaria parasites can be demonstrated in the blood when the spleen remains enlarged despite treatment with quinine, and—this is the point—becomes smaller again as soon as the bubo has begun to soften, then surely in view of the above frequency of 30 the symptom of splenomegaly should be considered significant in NICOLAS



565 Elephantiasis genitalis in Huguier Jersild's genito-ano-rectal syndrome
N.B Infiltration of the left buttock

(Sonck–Helsinki)



566 Infiltration and fistula formation in Huguier Jersild's syndrome.

(Sonck, Helsinki)



567 X ray photograph showing the narrowing of the rectum in Jersild's syndrome

(Lobe-Berlin)

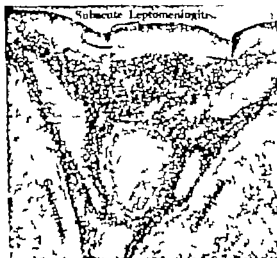


568 Human Jersild syndrome

(Sonck Helsinki)

FAVRE's disease. It goes without saying that the possibility of a *malaria-bubo spleen* should be kept in mind.

The *general syndrome* further includes *fever* which is usually slight, although it may rise to 40 °C (104 °F). The temperature falls gradually when the glands begin to soften in some cases not until they break through. In a relatively large number of cases the patients have slight pains in the joints but in some cases there may even be articular dropsy which may be followed by ankylosis and decalcification of the



569 Subacute lepto-meningitis in lymphopathia venerea.

(Hellerström–Stockholm)

bone. FRAUCHIGER and SONCK point to the fact that lymphopathia venerea may set up acute, slightly painful, intermittent swelling of the *[illegible]* (also in Europe!). The *liver* too may be enlarged; there may be *[illegible]titis*, a general malaise, feeling of distress, headache, and even *endocarditis*, *meningitis* and *encephalitis* are said to be possible complications (HELLERSTRÖM).

RAKE, EATON and STAUFFER found FREI's reaction to be positive in certain atypical pneumonias. RAJAM, DAVID and LOHRING have de

scribed *epileptiform attacks*, paraplegiae and lethal meningoencephalitis.

Gougerot and Carteau found *gummas* in lymphopathia venerea. Castinel and Reilly found leukocytosis and monocytosis. The blood sedimentation rate is slightly raised. There may be slight

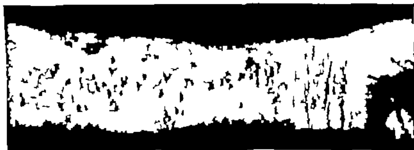


570. Papular rash due to sensitization to light by lymphopathia venerea. *(Saack, Helsinki)*

pressure of the spinal fluid, with increased protein content. In some cases again one may find an increased number of cells in the C.S.F. One should not, however, lose sight of the possibility that a patient with Nicolas-Favre's disease may also have neurosyphilis. A further

important symptom is *conjunctivitis* (usually unilateral), as in PARINAUD's conjunctivitis (CURTH and SANDERS), and *episcleritis periodica fugax*. HELLERSTRÖM even found conjunctivitis phlyctaenosa. SONCK, relapsing *iritis*.[1]

Exanthemata are, naturally, not so readily observed in coloured races, but they are more frequent than is evidently thought (SONCK). A very important point is that the patient, while the illness lasts, is highly photosensitive (SONCK). A papular eruption on those parts which are exposed to light may sometimes be one of the phenomena in NICOLAS FAVRE's disease (SONCK). Urticaria, erythema nodosum,



571 Papular rash due to sensitization to light in lymphopathia venerea.
(Sonck–Helsinki)

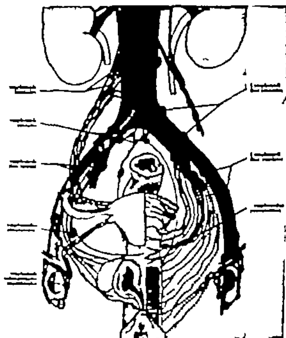
erythema exudativum multiforme, and even purpura have been found in some cases.

HELLERSTRÖM regards lymphopathia venerea even a "model disease" for the study of erythema nodosum, and SONCK has published an exhaustive study on this subject. Among nearly 1200 cases he found 10 % of the females and 1.7 % of the males having shown typical erythema nodosum. About a third of the female patients suffered from erythema nodosum while in the chronic phase (chronic process). In two thirds of all cases the erythema nodosum commenced in the bubo-stage. In about 10 % of the cases the erythema nodosum was preceded by sore throat. SONCK did not regard tuberculosis as having played a role in these cases, but perhaps syphilis has done so in some. The erythema nodosum was combined with joint symptoms in nearly half of the cases, solar dermatitis occurred

[1] HELLERSTRÖM states that the conjunctivitis which has been described by PARINAUD was most probably due to tularaemia.

in 77 % of the female cases and in a few cases also erythema exudativum multiforme was seen. The FREI test was usually more pronounced in those patients with lymphopathia venerea who suffered from the additional erythema nodosum.

Both medicamentous and syphilitic exanthemata may be confused with those accompanying lymphopathia venerea. The hyper-photosensitivity described by SONCK, which he found in 50 % of his chronic cases, is of great importance. In the subacute cases, 30 %



572. The lymphatic system of the female genitals.

(Loke-Berk)

of the women and 12 of the men had become hypersensitive to light. Here follow SONCK's own remarks:

"Photosensitivity in lymphopathia venerea begins to manifest itself about 9-10 weeks after the infection, i.e., on an average 5-6 weeks after the appearance of the bubo. The phenomenon disappears again after recovery. In chronic cases of proctitis and ulcera chronica vulvae

etc. this photosensitivity may last as long (*i.e.* as many years) as the morbid process itself During the summer "solar eruptions" appear sometimes over a period covering as many as ten summers The exanthema is seen almost exclusively on the uncovered parts of the skin, *e.g.* the face, the lower arms and the neck-sternum triangle. In some cases the exanthema is erythematous in others, either papular or urticarious Eczemas have not been found but hydroa vacciniforme was observed which left scars and pigmented patches. Photoconjunctivitis was observed in some cases synchronously with the dermal phenomena.

Apart from itch, the patient may be troubled with restlessness headache and vertigo. It is strange that photosensitivity has been observed—or, at any rate, described—less often in the tropics, since there was no evidence whatsoever in Finland, of any preference for the fair as against the dark type HAXTHAUSEN has called attention to the fact that some exanthemata show more, and others, less "affinity" for either cold or warm parts of the skin for instance, the syphilitic exanthema for the warm, and the acneiform tuberculide for the colder parts Maybe this phenomenon, too is related in some way to the influence of light.

The course of the disease may last a couple of months before the bubo either breaks spontaneously leaving an "after-fistula" or, maybe, gets better without breaking through. According to CAMINOPETROS, the disease may remain latent, in women, as long as two years In men, SIMONS found an average duration of the disease of six weeks, which, by adequate treatment, could be reduced to a fortnight. The patient may recover without further complications—except for the remaining ugly scars— but in some cases the disease may lead to chronic *urethritis epididymitis* chronic *proctitis* and especially JERSILD's *syndrome* referred to above The present writer never saw lymphangitis with bubonuli penis (known as "*peralymphitis*") this has perhaps been confused with lymphangitis in ulcus molle, which may occur either alone or in conjunction with NICOLAS FAVRE's disease.

WASSERMANN's reaction is positive when the disease is complicated by syphilis. In women with JERSILD's syndrome one sees, moreover the so-called *fishmouth-urethra* and *bartholinitis*

Both *perimetritis* and *salpingitis* it seems, are possible complications.

PATHOLOGY

The histology includes oedema, granulations, fibroblasts epithelioid cells, plasma cells giant cells and small necrotic gummas and abscesses containing *"gamma bodies"* The surrounding tissue has a tuber



5̃73 Biopsy of the adenitis in lymphopathia venerea reveals numerous foci, lying mostly peripherally Note peripheral light zone with epithelioid cells.

(Hellerstrom–Stockholm)



5 4 I nd mall bscesses surrounded by epithelioid cells.

(Hellerstrom–Stockholm)

culoid structure. (Annales de Dermatologie, June 1949 contains an exhaustive study by FAVRE.)



575. Central abscess from marked spot of former picture. Note palisade formation of the epitheloid cells.

(Hellerström—Stockholm)

THE PRIMARY LESION

Many attempts have naturally been made to discover the primary lesion, the "porte d'entrée" of lymphopathia venerea, but thus far without undoubted success. The present writer found no specific primary affection in over a hundred male patients 20 % of these patients had had an unspecific lesion of the penis 2 % had balanitis one man had herpes genitalis, and 12 had, just previously either ulcus molle or primary syphilis Two per cent. of the men had non-gonorrhoeal urethritis—which might, perhaps, pass for "*urétrite lymphogranulomatique*" but no typical primary lesion could possibly be found. HELLERSTRÖM and WASSÉN in 53 % of their cases, CASTELLO D VALLO in 29.4 % and SÉZARY and DRAIN in 54 % found what they called a "primary lesion" at any rate a genital morbidity such as herpes or ulcer but these figures appear to be high.

PITTLACTOS has described four types of primary affection, e.g. papule, ulcer node and urethritis but this classification has not met with much agreement among those whose work has made them familiar with the disease



576. Scar of a primary lesion
(Sonck–Helsinki)



577. P[illegible] [illegible] of lymphopathia venerea in the coronary sulcus.
([illegible])

REACTIONS

1. Frei's *cutaneous* [illegible] The most important reaction in lymphopathia venerea is [illegible] Frei's cuti reaction which, according to

FLANDIN and TURIAF fails in only 3 % and according to CASTELLO D AVANZO in 4½ % of cases.

The reagent is prepared as follows. From a softened part of a bubo —in which distinct swelling of the iliac lymphatics, but no primary affection (beware of mixed infection with syphilis or ulcus molle) is found—pus is aspirated through a thick needle, and strained 5–10 times in saline solution. A few drops of a 5 % carbolic acid solution are added, after which the reagent is heated for two hours at 60° C, and again next day for one hour at the same temperature, when it is ready for intracutaneous injection. Its antigenic properties are unequal the antigens of mice brains and chicken embryos are much more stable but since they are not 100 % specific they necessitate control tests with avirulent but otherwise corresponding material. It is advisable to test the antigen before use, by injecting it into one or two patients whose diagnosis is not in doubt and if prepared from pus, to examine it microscopically beforehand.

Intravenous injection of the antigen causes fever (according to CASTELLO D AVANZO, in 86 % of cases) which, according to RAVAUT is definitely indicative of lymphopathia venerea.

The following details must be kept in mind

(a) FREI's reaction does not turn out positive until at least two weeks after the onset of the disease. In rare cases this pre-allergic" phase may be as long as three months (SONCK)

(b) In fever secondary syphilis, and when a soft chancre is present, the reaction may remain negative for a long time.

(c) The reaction can be read after 24 or 48 hours but in some cases there is another late reaction which does not appear until a week or a fortnight afterwards.

(d) A negative result is a more important indicator than a positive one.

(e) In the absence of clinical phenomena the diagnosis should not be based on FREI's reaction alone.

(f) For JERSILD s syndrome, however FREI s reaction is usually the only existing diagnostic aid. In the early phase, iliac lymphadenitis is as a rule, a more reliable symptom than FREI s reaction.

(g) Apart from the contents of a bubo, pleural, articular or spinal fluid may also be used for this reaction.

(h) Even in the absence of clinical phenomena, FREI s reaction was

test (serum dilution 1:40) in 93% of patients with clinical lymphopathia venerea. But 7.4% of syphilitics in various stages were also positive and 26% when the serum titer was at least 1:5.

DIAGNOSIS

NICOLAS FAVRE's disease must be differentiated from syphilitic bubo, chancroid, pyoderma, scabies penis, tuberculosis, HODGKIN's disease (general lymphadenosis, cachexia, Sternberg's cells), carcinoma hernia, epididymitis in cryptorchismo ("cryptorchitis") and, especially, from bubonic plague; further from varices (which, however, are located in the thigh), sporotrichosis and lymphatic varices in filariasis. None of these diseases shows a positive FREI's reaction, and, excepting HODGKIN's disease, plague and tuberculosis, none is coupled with iliac lymphadenitis.

THERAPY

In 25% of cases rest in bed was alone sufficient to bring about spontaneous recovery without the gland breaking through. In these cases the illness lasted between one and two months. Patients receiving a course of treatment with sulpha fuadin in the early stages of the disease may often be discharged within 2–3 weeks. Relapse, however, is possible as soon as a month after recovery. KRIJNEN treated his patients with sulphanilamide fuadin for 5 (minimal) to 23 (maximal) days, and found 25% relapses within three months. HURWITZ, with an average duration of treatment of 22 days, had 10–12% relapses.

Once a distinct softening process is found to exist, either incision or puncture will usually be necessary.

The following is a useful plan of treatment.

During the first and second stages, daily injections of 5–10 ml of the patient's own blood, coupled with 1 or 2 tablets of sulphathiazole or sulphadiazine per os 5 times a day for the first week.

If either fuadine or anthiomaline is available, one of these is substituted for the autohaemotherapy. An adult male patient is given 1½ ml fuadin (13.5% trivalent antimony preparation) the first day, 3½ ml the following day and a full 5 ml ampule on the third day. After this, a 5 ml injection is given every two or three days until the quantity administered totals 40 ml. In general, there will not be any addition

al phenomena, apart from a slight sickness and, in some cases a little diarrhoea but these are no indication to discontinue the treatment.

In the third stage when pus is clearly present which will never be resorbed, incision or puncture may be desirable. After puncture the gland is washed out with the contents of an ampoule of soludagénan (soluble sulphapyridin) or any other non-irritant disinfectant. HELLMANS and HELLERSTRÖM both advocated also a series of injections of FREI s antigen, but this method has not been adopted to any great extent.

Penicillin is ineffective. The most recent antibiotic of which favourable results are being recorded is aureomycin. It is injected intramuscularly 10–40 mg daily in a 2 ml physiologic saline solution. *Aureomycin* may also be taken per os, viz 300 mg every 4 hours. It is said to act favourably also in cases of granuloma venereum. In some cases aureomycin causes slight hypochromic anaemia, which, however, responds favourably to folic acid (WRIGHT and co-workers) *Chloromycetin* too appears to be effective (1–3 g every 8 hours, 3 times per 24 hours, for 2 weeks)

In certain cases the scars can be excised.

Strictures may be dilated if possible, however surgical treatment is preferable. Extirpation of the entire bubo may result in elephantiasis of the leg and the scrotum.

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LYMPHOPATHIA NON VENEREA

In his book on venereology and genitopathology (1947), the present writer described a form of non venereal inguinal lymphopathia, coupled with periadenitis, multilocular softening and iliacal lymphopathia, in which FREI s inverted test turned out negative. The case was observed in a P O W who had been isolated for four years. We were here faced with one of three possibilities (a) a patient who had become infected while escaping (but this it appeared, could not have happened) (b) a case of NICOLAS FAVRE s disease which had remained latent for over three years and was now manifesting itself, or (c) a pyogenic lymphopathia inguinalis suppurativa multilocularis with slight iliacal adenitis The last named possibility seemed to be the most likely

THE MILIARIA GROUP OF DERMATOSES AND TROPICAL ACNE

CHAPTER 32

THE MILIARIA GROUP OF DERMATOSES (INCLUDING PRICKLY HEAT)[1]

WALTER B. SHELLEY – Philadelphia
R. D. G. PH. SIMONS – Amsterdam

Numerous dermatitides have always been a scourge of the tropics The sweat gland has been indicted in some of these for centuries However only recently has it been possible to delineate rather precisely the role of the sweat gland and sweating in tropical skin disease. As a result of clinical and laboratory research our concept of the role of the sweat gland has at once been expanded and simplified. Numerous dermatological terms have lost significance by becoming synonyms. The major advance has been in the widespread recognition that obstruction to the free flow of sweat commonly occurs, with a resultant retention within the skin of trapped sweat. This sweat retention manifests itself clinically in various forms, yet fundamentally we are dealing with a sweat retention disturbance which probably is best termed *miliaria* Nevertheless, it is possible, and at times advisable, to classify miliaria on the basis of simple distinctive clinical differences into four major types, as will be indicated below

DEFINITION

Miliaria is the generic term for a group of disorders of the skin *due to sweating in the presence of an obstruction in the sweat duct* It may be either *primary* arising de novo on normal skin, or it may be a *secondary* complication of many dermatitides.

[1] These observations in part were made possible by a research grant of the United States Public Health Service (R G 330 1947-51).

The morphological types of miliaria are to be distinguished on the basis of appearance or on the histological site of sweat retention. In the interest of uniformity the following scheme of nomenclature will be used in this chapter

Miliaria crystallina (vesicles of sweat trapped in stratum corneum)
Miliaria rubra (papulo-vesicles of sweat trapped in epidermis)
Miliaria profunda (papules of sweat trapped in dermis)
Miliaria pustulosa (pustules of sweat trapped in epidermis).



580 Prickly heat

A brief listing of synonyms may be helpful but it should be realized that many authorities in the past vigorously opposed some of this synonymy. It is only now possible to reconcile the divergent claims and thereby simplify terminology. *Miliaria crystallina* was also termed

[1] Pustula [illegible]

sudamina and *miliaria alba*. *Miliaria rubra*, the most widely recognized and described, of course merits the largest group of designations including many strange native tribal names. Some of these often employed are *prickly heat*, *lichen tropicus*, *heat rash*, *red gum*, *miliariasis*, *sudamina*, *tropical eczema*, *dermatitis hidrotica* and even *strophulus*.

A consideration of certain of the European terms is interesting. The German designation *rote hund* conjures its clinical semblance to canine scabies; the French *gale bedouine*, *gale Iluvis* also relate to scabies, whereas the synonym *impetigo miliaire* and also *bourbouilles*



581 Prickly heat.
(*Fasal-Sen Γ mdsto)*)

refers to infection; the Italian term *calori* emphasizes the aetiological role of elevated temperatures. The synonymy of *miliaria profunda* consists of *anhidrotic heat rash* (seen in anhidrotic asthenia), *mammillaria* (clinical resemblance to breast), *miliaria alba* (a white papular lesion) and *hidrocystoma*. *Miliaria pustulosa* is also known as *pustular miliaria*, *impetigo miliare*, *miliaria papules* and *periporitis*.

It is too much to hope that a simple designation *miliaria* can replace the numerous titles used, but at least it can be hoped that it will be recognized that all these are but variants of the basic picture of sweat retention.

SYMPTOMATOLOGY

Miliaria crystallina is a non-inflammatory eruption of small, superficial, crystal-clear vesicles containing sweat. They are exquisitely delicate and superficial, appearing as dew drops on normal skin. There is no observable clinical anhidrosis since only a small number of the glands is affected. Completely asymptomatic, they are rarely seen by the patient or physician since slight friction by a towel or



582 Experimental miliaria rubra. Wet gauze was kept for 3 days. Two days later after 3 hours of sweating in hot room (96° F) this picture was taken. Surrounding skin was normal.

clothing erases them, without trace. They may occur anywhere on the body and appear only after sweating is induced. Most commonly they are seen in hospitalized patients exhibiting in addition to fever a certain degree of immobility, thus insuring no damage to these fragile lesions. They usually occur in sunburned areas in normal subjects during exercise, sometimes being confused with the primary vesiculation of actinic injury. Interestingly localized patches of

miliaria crystallina may be seen in sweating subjects at the sites of minor epidermal injuries, such as follow prolonged wet compresses, application of adhesive tape, or minor irritant topical medicaments. Furthermore this secondary type is seen also in areas of dermatitis, providing the secretory coil remains functional.

If untouched the vesicles disappear spontaneously in a few hours or days, depending upon the activity of the sweat gland.

Miliaria rubra is a common pruritic and inflammatory papulovesicular disorder. It manifests itself most often as small red elevated papules on erythematous skin. The papules are not follicular, and remain discrete, never becoming confluent. Miliaria rubra may also



583. Anhidrotic skin of the right shoulder in tuberculoid leprosy unaffected by prickly heat.

appear in the form of small clear tense vesicles showing erythematous halos. Typical miliaria crystallina lesions may also be seen, reflecting the basic common denominator of these two variants of sweat retention.

Many of the papules may develop tiny vesicles or pustules at their apices. Later the lesions involute with mild desquamation. Also evidence of a *concomitant* true folliculitis may be present. The lesions of miliaria rubra are not truly pruritic; rather the sensation is that of a tingling burning or pricking. The patient's desire is to rub the affected areas more than to scratch them. Scratch marks are rarely seen. The

prickling sensation is aggravated by anything which causes sweating and disappears completely upon the cessation of sweating The affected areas usually show hyperidrosis or normal sweating although in the later stages of severe miliaria rubra demonstrable localized anhidrosis is the rule.

The sites of predilection are the antecubital and popliteal fossae, the chest, abdomen, and all the areas of friction (belt, straps, wrist watch) It is never seen on the palms or soles, although it may occur anywhere else. Interestingly the face is often exempt. Although usually bilateral and symmetrical miliaria may be seen in unilateral areas, *e g* in individuals sleeping on one side only Miliaria rubra does not occur in any area in which the sweat gland is absent or not functional *e g* in leprous patients (Fig 583) in patients with congenital ectodermal defect, or in sympathectomized areas

The incidence of prickly heat is very high in people living in tropical areas or working in any hot environment It is also very common in infants who are over-clothed by solicitous mothers. The individual susceptibility varies but some observers state that essentially all are candidates for this disease. SULZBERGER and EMIK reported that 66% of several hundred men studied by them on Guam had some miliaria rubra Although numerous authors attest to special factors affecting the incidence of miliaria rubra SULZBERGER could find no evidence of racial, sexual or hereditary pre-disposition, nor did the complexion or weight appear significant Conflicting views are also to be seen in the literature regarding the effect of salt and water intake on the severity of prickly heat The effect of suntanning is unpredictable in some it had a definite beneficial prophylactic effect, in others it predisposed to miliaria Further controlled observations are needed on the precise effects of such simple factors Adequate data are lacking

The course of miliaria rubra varies. Although a latent period of two to three days is an absolute requisite for the development of miliaria rubra, an individual may spend months in the tropics before the disease appears The basic trigger factor is a period of several days of practically uninterrupted high environmental temperatures Invariably the miliaria subsides within hours of removal of the patient to a cool climate or environment. The rapid abatement of symptoms is followed in days by resolution of the skin changes Exacerbations are common,

and they coincide with increases in the work load or in the *effective temperature* of the patient's environment. It should be noted that it is the effective temperature which controls the pattern of events. Actually miliaria may involute in the presence of an increasing dry bulb temperature. This is due either to a significant drop in the humidity of the environment or in the activity of the patient.

Complications are usually seen in the form of secondary infection (folliculitis pyosis, furunculosis) eczematous contact dermatitis due to allergic reaction to topical treatment, and intertrigo. Candida albicans may at times be readily isolated from areas of prickly heat, but it is doubtful whether they are of significance or of the pathogenic type.

Miliaria profunda is the cutaneous change seen in patients suffering from *anhidrotic heat exhaustion* (HORNE and MOLE), tropical anhidrotic asthenia (ALLEN and O'BRIEN), thermogenic anhidrosis (WOLKIN, GOODMAN and KELLEY) heat exhaustion, type II (LADELL, WATERLOW and HUDSON). The affected skin is uniformly studded with multiple discrete flesh-coloured papules which show a sweat pore localization. None are surmounted by the hair follicle. These papules dramatically increase in size whenever vigorous sweating is induced. At times it is possible to demonstrate free fluid within the papule by simply pricking it with a needle. Casual examination may fail to reveal the presence of this type of miliaria. Oblique lighting is generally most satisfactory. The distribution of miliaria profunda is widespread, frequently involving the trunk, arms and legs. The face, hands, feet, axillae are exempt usually.

It may persist for varying lengths of time; usually however residence in a temperate climate produces complete resolution of all the lesions in from several weeks to several months.

The skin changes in miliaria profunda are non-inflammatory and symptomless except for the presence of a partial or complete local anhidrosis. Widespread miliaria profunda is accompanied by a compensatory hyperhidrosis of the face, a point of additional aid in diagnosis.

O'BRIEN found that the application of anhydrous lanolin to patches of miliaria profunda restored normal sweating in the treated areas. This he termed the "*lipoid response*".

Miliaria pustulosa is a pustular sweat retention dermatosis which ordinarily develops secondary to some other skin damage which has produced injury, destruction, or blocking of the sweat duct or pore. It has been most carefully studied by LOBITZ who has observed it associated with acute or chronic contact dermatitis, urticaria, localized neurodermatitis, intertrigo and lichen planus. It is seen most commonly in the summer season or whenever the weather is hot enough to induce sweating. However, it may occur in any season or climate if an occupation, activity, or state of health induces sweating. It has been observed in both sexes and in all age groups. It was formerly felt to be limited to children, the term *periporitis* being in popular usage.

The lesions of pustular miliaria are distinct, discrete, superficial pustules *not* associated with hair follicles. The purulent material is white, and it is well to note that the dark punctum at the apex of the pustule, often mistaken for a broken hair, is the hyperkeratotic plug in the sweat gland orifice. The lesions are pruritic, and like miliaria rubra lesions, the pruritus waxes and wanes in close association with the presence or absence of sweating.

The lesions are usually sterile or may contain non-pathogenic micrococci. Usually if a pathogenic organism (staphylococcus aureus) secondarily invades the lesion, it assumes a yellowish tinge. Other types of miliaria may be present, and this aids in making the clinical diagnosis.

The pustules may be in any area of skin that has been previously inflamed and will always be limited to those areas.

MEDICAL CONCOMITANTS

Miliaria crystallina has no bearing on the patient's state of health, although it is seen frequently in hospitalized febrile patients.

Miliaria rubra – none.

Miliaria profunda, when generalized in distribution, may produce a significant generalized anhidrosis. This manifests itself in the clinical syndrome of *tropical anhidrotic asthenia* with the abundant signs and symptoms of heat intolerance. These individuals show a tendency to overfatiguability, irritability, anorexia, inability to concentrate and drowsiness. Headaches and vertigo are noted by some. During

physical exertion, acute signs of heat intolerance develop suddenly moderate elevation of temperature, palpitations, increased respiratory and pulse rate, nausea, polyuria, feeling of impending disaster, and finally collapse. The skin in the affected areas remains hot, but dry



84 Biopsy of prickly heat The circle represents a micro-abscess in direct communication with the duct of the sweat gland.

These symptoms rapidly disappear when the patient is removed to a cool climate or environment.

Miliaria pustulosa – none.

PATHOLOGY

Miliaria crystallina presents vesicles in the stratum corneum overlying sweat ducts. No other changes are seen.

Miliaria rubra shows a distinctive and often diagnostic histopathological picture Hyperkeratotic and parakeratotic plaques and plugs are seen obstructing the terminal sweat duct. Vesicles are seen in the epidermis which on careful study with serial sections usually may be shown to be in direct communication with the sweat ducts. Many

of the ducts show dilatation. The corium may show oedema, and invariably presents dilatation of the vascular channels with a lymphocytic cellular infiltrate about the sweat ducts, especially near the dermal epidermal border. The sweat gland acini and all of the other cutaneous appendages are completely normal.

Miliaria profunda shows changes more elusive. The terminal sweat duct is replaced by a obstructing keratin plug which lies deeply embedded in the epidermis. The sweat duct shows evidence of rupture at the dermal-epidermal border and at this site is seen a localized intense periductal oedema which corresponds to the papule seen clinically. In certain examples, *e.g.* hidrocystoma, the duct does not rupture, and the sweat is seen trapped within dilated ducts. The blood vessels and lymphatics are moderately dilated and the dermis as a whole is oedematous. Lymphocytic infiltrations may be seen perivascularly.

It is difficult for the pathologist in both miliaria rubra and profunda to capture the full complement of changes since after a biopsy is taken, fluid redistribution is extremely rapid. This is especially true in miliaria profunda where we have had occasion to study many slides showing no changes whatsoever.

Miliaria pustulosa (Fig. 584) shows an intra-epidermal pustule containing an exudate of neutrophiles, lymphocytes and fibrin. Serial sectioning may reveal a sweat duct in direct communication with the base of the abscess. There is never any association with hair follicles.

AETIOLOGY

It is now possible as a result of extensive clinical and experimental studies to unify these miliarias on the basis of a common pathogenesis. The prime feature is sweat retention. *The sweat is secreted into instead of onto the skin.* The prime aetiological factor in the pathogenesis of the miliarial group is minor non-specific epidermal injuries of various types which lead to abnormal keratinization producing an obstructive keratinous plug in the sweat orifice. The most common and significant injury is prolonged maceration of the skin with sweat. Thus is the usual antecedent of miliaria crystallina and rubra. However, miliaria profunda is usually preceded by prolonged miliaria

rubra which by repeated local inflammatory changes produces a deep keratinous plug. In the case of miliaria pustulosa the keratotic plugging is produced by the inflammatory changes of the preceding dermatosis. It is possible that such skin readily reacts with a leukocytic response, explaining the pustular nature of this miliaria.

The clinical manifestations result from the level at which sweat escapes into the skin.



585 Plugged and dilated sweat duct with periductal circles. The biopsy was taken 1 day after 1 hour of sweating. No evidence of rupture of duct in serial sections.

Miliaria crystallina	stratum corneum	no symptoms
Miliaria rubra or pustulosa	epidermis	pruritus
Miliaria profunda	dermis	no symptoms

A brief review of the experimental work in this field aids in the elucidation of the pathogenesis of miliaria.

Miliaria crystallina. SHELLEY and HORVATH found that miliaria

crystallina could be experimentally induced in man by a superficial injury by any of the following means: maceration (wet gauze pad on skin for several days), application of adhesive tape for 1 to 10 days, application of such chemicals as aluminum chloride, phenol, chloroform, superficial thermal burn, superficial injury by freezing (solid CO_2) or ionophoresis, abrasion with sandpaper and mild sunburn (ultraviolet light). On the basis of physiological and histological study it appeared that the non-specific epidermal injury produced an obstructive hyperkeratotic plugging of the sweat duct orifices. Upon stimulation of the sweat gland, sweat retention as well as anhidrosis miliaria crystallina-type vesicles resulted. This work is in keeping with many well known clinical findings and it has been confirmed by PECK in regard to adhesive tape, and by THOMSON in studies on the effect of ultraviolet light.

Miliaria rubra was first experimentally achieved in man by SMITH in 1927 by applying to normal human skin cultures of a yeast like fungus he had isolated from the scales of patients who had miliaria rubra. After an incubation period of four days miliaria crystallina and rubra lesions appeared in the treated sites. He did not relate the changes to the sweat gland, but rather felt prickly heat was a fungous infection of the skin. O'BRIEN has produced miliaria rubra by the application of kerosene, saline compresses or cultures of staphylococcus aureus. It is his feeling that miliaria rubra is a manifestation of primary staphylococcal infection of the skin. SHELLEY and HORVATH have also produced experimental miliaria rubra. On the basis of their study it would appear that a single superficial epidermal injury of various types invariably induced hyperkeratotic plugging of the sweat duct with consequent sweat retention anhidrosis. In susceptible subjects thus prepared, a single heat exposure of several hours led to disorganization of the upper end of the sweat duct due to pressure of entrapped sweat. This manifested itself clinically as miliaria rubra each time sweating occurred apparently by permitting the flow of sweat into the epidermis. SULZBERGER, HERMANN, KELLER and PISHA have further broadened our concept of the manifold aetiological factors in this disease by producing experimental miliaria rubra by the application of electrically positive agents to the skin surface. They used various surface active agents as well as lithium iodide

Miliaria profunda was reproduced experimentally in cats in 1970 by SCHIDACHI. He induced sweating in glands in which the duct orifices had been removed surgically. Recently SHELLEY has described experimental miliaria profunda in man. He produced selective destruction of the epidermal and upper dermal sweat in normal human skin with a resultant obstructive keratinous plug forming in the ductal area. This was attained by means of superficial electrodesiccation after inserting a fine needle into the sweat duct pore area. Upon stimulation of sweating the clinical findings of miliaria profunda appeared. Histopathological and pharmacological studies indicated that sweat retention had occurred in the dermis to produce this change.

Miliaria pustulosa has been experimentally duplicated by O'BRIEN in his studies on the effect of topical application of staphylococci on the normal skin. Thus various investigators have been able to duplicate experimentally all of the types of miliaria which occur clinically as primary or secondary dermatoses.

DIAGNOSIS

Miliaria crystallina is not readily confused with any other dermatoses in view of its unique appearance.

Miliaria rubra. At times consideration must be given to rule out seborrheic dermatitis, contact dermatitis, scabies, and varicella. The cardinal specific sign in miliaria is the exacerbation which occurs upon sweating.

Miliaria profunda. Here care must be taken that the lesions are not missed in examination. Goose flesh or a papular urticaria may resemble this process, but simple observation usually enables one to distinguish these clearly.

Miliaria pustulosa. This is readily misdiagnosed as folliculitis. A study of its appearance and localization aids in preventing errors of this sort.

The hallmark of the miliaria group is the history of a papular vesicular or pustular eruption becoming more prominent in the presence of a stimulus to sweating. The usual triad of findings, appearance, localization and history, are of great help in establishing a diagnosis. A biopsy should be taken in questionable cases. It must be emphasized that any or all of these different types of miliaria may

occur as a complication of some preceding or primary dermatitis.

Finally note should be made of a simple pharmacological test too rarely used in the study of the patient suspected of having miliaria. It consists of the intradermal injection of atropine sulphate solution (1 ml of 0.01%) in the dermatic area. In the presence of miliaria, heating will cause a flareup of the adjacent sites, but none in the atropinized site since here the gland is inactivated and sweat retention eliminated.

THERAPY

Probably nowhere in medicine are there as many vigorously proposed "cures" as in this particular field. As conspicuous as the abundance of claims is the absence of controlled observations. The very nature of this disease, so intimately tied up with heat loss and heat production, insures a widely fluctuant course. Tropical physicians, dermatologists and the public alike each have a "*special*" cure, usually based on a faith founded during treatment undertaken at the beginning of a fall in *effective* temperature or rest from work.

The fundamental principle of therapy for all types of miliaria is the elimination or reduction of the need for sweating. Much can be done to reduce the heat load. The simple improvement of ventilation with a consequent drop in humidity is indicated. The use of fans to increase evaporative heat loss and to reduce sweat maceration is valuable. The ideal approach is *air-conditioning*. Many patients find complete relief from miliaria by the single expedient of having a small air conditioner unit in their bedrooms. Numerous observers have found that daily 8-hour periods in a moderate environment prevents miliaria. The prevention of miliaria is in essence the cure, since it is a self limiting disease. In the case of troop personnel with a special susceptibility to miliaria, transfer from the tropics may be indicated.

Cool light weight clothing aids in reducing the heat load. This may be especially applicable in the case of over-dressed infants in over heated homes. Further controlled studies on the effect of various fabrics on the incidence of miliaria are urgently needed.

The reduction of internal heat production is also of significance in the control of miliaria. Usually this is achieved most satisfactorily by reducing the work load. Or if this is not possible directly it may

be feasible to alternate periods of work and rest, permitting some drying of the skin during the latter periods.

Reduction of sweating should not be attempted by the use of drugs such as atropine, since this may lead to dangerous heat intolerance with consequent hyperthermia and collapse. The patient should be advised not only to avoid the prolonged macerative effects of sweating but also avoid other agents injurious to the epidermis. This includes over-bathing excessive use of soap use of detergents in bathing the use of irritant topical medicaments, and clothing or accessories causing friction.

The role of fluid and salt intake in relation to the severity of miliaria rubra is in dispute. Various observers have recorded conflicting data on this interesting facet of therapy Further study is needed.

To turn to the common delight of the afflicted, namely topical remedies, very little can be said that should merit attention. In the absence of continued stimulus to sweating the epidermis rapidly desquamates and exfoliates the plug with restoration of normal skin. There appears to be not a single controlled therapeutic study of the effect of topical treatment. Yet, tons of powders, lotions and ointments are used yearly to combat miliaria. It is doubtful whether any beneficial effect is achieved by this wholesale onslaught on the obstructive culprit whose natural unmolested life cycle is a short one. All of the medicaments moreover are two-edged swords since any irritative effects are rapidly translated by the skin into more obstructive keratinous plugs No systemic therapy is indicated.

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TROPICAL ACNE

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DEFINITION

Tropical acne is a form of acne because it is characterized by comedones, cysts and pustules. It differs from ordinary acne in the following ways (1) Its onset is sudden among white people subjected to a tropical climate (2) It affects an older age group. (3) The eruption most frequently affects the chest and back. The face is not commonly involved as in acne vulgaris. The buttocks and thighs are sites of the disease in a high percentage of cases. (4) The eruption itself is characterized by large pustules by draining sinuses, many of which are intercommunicating and by the formation of plaques. (5) These lesions on healing leave extensive disfiguring scars which are frequently keloidal.

HISTORY

Tropical acne was known before the war among the whites living in the tropics but because there were so few of them, little attention was paid to this disease. During the war with large movements of troops to the tropical areas particularly the South Pacific, the dermatologists there soon realized that they were seeing an unusual form of acne. It presented one of the most serious dermatological problems in this area. COHEN and PRATT, KLEY and MCLAUGHLIN all were struck by this fact. Tropical acne was second in incidence to fungous infections. Twenty eight and a half per cent of all patients with der

matological diseases arriving from the Pacific area had tropical acne Fungous infections made up 29 4 % of the total This disease was found to be so disabling that the patients had to be returned to a cooler climate before their disease could be controlled.

AETIOLOGY

Because tropical acne presented such an unusual picture and because it was so disabling several studies have been carried out to determine its aetiology SULZBERGER and NOVY independently have published a series of cases with a total of 151 patients. They found that the average age of onset was 22.5 years which is considerably older than that of the onset of acne vulgaris. In attempting to determine the relationship between a previous acne and tropical acne, the cases were reviewed and while most patients have a history of having had a mild acne consisting of a "few black heads and pimples" there were only very few who had had a previous serious acne vulgaris. It was felt, therefore, that this condition was not an exacerbation of the previous acne vulgaris but a different type of acne

One of the striking characteristics of tropical acne is its sudden onset upon going to the tropics Most of the patients developed a severe form of the disease within six months after arriving in that area.

Tropical acne usually involves the trunk In the series of 151 patients 126 had involvement of the back and 87 had involvement of the chest and abdomen. Only 42 had involvement of the face Thirty six had severe involvement of the buttocks and thighs

There appears to be a definite racial predisposition to this disease American Negroes serving among the troops in the tropics, under the same conditions as the whites, seem to have escaped the affliction In addition this condition is not described among the natives of the tropics

Tropical acne is not limited to the male sex as a few cases have occurred among the nurses and other women in the services. These cases were typical and severe.

Psychogenic factors While acne vulgaris can be exacerbated by emotional upsets stresses and strains there was no increase in the incidence of the disease among neuropsychiatric patients who were seen in large numbers during the war

Living conditions Tropical acne occurred not only among those enduring the hardships of the front lines but was commonly seen among the troops stationed at bases where the living conditions were excellent and among men aboard ships with adequate bathing facilities. The diet of these military men was well balanced so that a dietary deficiency could not have caused the disease.

Careful investigation was carried out ot determine whether the type of duty was responsible for the disease. It was found that three



586. Tropical acne involving the back. While acne conglobata is a chronic disease tropical acne is an acute condition.

quarters of the patients had clean duties, such as guards mailmen, radio operators and pharmacists assistants. Only one quarter of the patients were performing greasy and dirty jobs. It is therefore obvious that the work itself did not produce the disease. This observation shows that tropical acne is not variant to occupational or oil acne.

Another study was done to determine what affect clothing and tanning of the skin had on tropical acne. It was found that neither the wearing of clothes nor tanning of the skin prevented the disease from occurring As to the blood chloride, this was not increased in

comparison to 50 controls with clear skins chosen from the same drafts of men.

After taking these many factors into consideration there seems to be only one common factor which could account for this disease and that is the effect of the climate itself. The heat and humidity produces an over activity of the sebaceous glands which results in plugging of the sebaceous ducts and leads to comedones and cyst formation. Secondary infection readily takes place producing pustules and pyoderma. This in turn results in the production of ulcerations and *granulomas which cause scarring on involution.*

The fact that extreme heat and high humidity are sufficient to produce this kind of acne in individuals with an acne or seborrheic diathasis is further suggested by the observations on prickly heat and thermogenic anhidrosis The histological studies on patients with prickly heat by SULZBERGER and ZIMMERMAN clearly show that the orifices of the sweat glands are plugged with plaques of squamous epithelial cells Behind this plug is found a distention of the ducts with a cellular inflammatory response in the cutis. These changes are explained on the basis that continual sweating causes a maceration of the surface of the skin and faulty keratinization resulting in the filling of the sweat glands with cellular debris. The same histological changes are found in patients with thermogenic anhidrosis.

From these investigations it is reasonable to assume that the same process happens to the sebaceous glands They are subjected to the same macerating effect to the skin and the epithelial cells can fill the orifices of the glands causing comedone formation and cysts Later these can become infected to produce pustules and pyodermic lesions.

SYMPTOMATOLOGY

On observing patients with tropical acne one is immediately struck by the severity of the disease. While deep-seated cystic acne is occasionally seen among patients with acne vulgaris in temperate climates this type of eruption is the rule among those with tropical acne.

The ordinary papules of acne are not often observed because the lesions of tropical acne are larger and better described as nodules. The lesions first appear associated with comedones as a simple retention cyst with no change in the overlying skin and they gradually

become larger and then secondarily infected. They later become very painful In many patients the entire upper back and chest are entirely studded with these lesions. These form large plaques. The plaques may have many draining sinuses which inter-communicate. Pressure at one point can cause a discharge of pus several centimeters away These are so painful that the wearing of bandages and dressings is extremely uncomfortable. Many of the patients find it impossible to carry on their duties. After the nodules open they may drain for many weeks, and as the drainage becomes chronic the exudate becomes



587 Tropical acne in ol ing the thighs. Careful investigation showed that it is not anent to occupational or oil acne

yellowish with an oily gelatinous consistency At times there can be an increase in drainage due to the subcutaneous channelling of a purulent material from a neighboring lesion. As the discharge lessens, healing will begin to take place with the area filled in with granulating tissue after which there is scar formation. Keloid formation is very common. About the face and neck many patients develop long linear keloids and are badly disfigured in much the same way as women who have had pyoderma faciale Some of these are 8 to 10 centimeters long Around the chest and shoulders extensive hypertrophic scarring is frequently seen. In some of the patients there are hand-sized areas

of scarring In some instances these large areas have bridges of normal tissue with comedones like those described as characteristic of acne conglobata.

Tropical acne has several features in common with acne conglobata. It is however an acute disease, while *acne conglobata is a chronic one taking years to develop* The sites of involvement, the large double comedones, the formation of plaques, with numerous fistulous openings are characteristic of both diseases Also they both involute with severe hypertropic scarring *Tropical acne improves when the patient returns to a cooler climate*

PATHOLOGY

The microscopic findings in tropical acne are similar to those of severe acne vulgaris. The comedone shows dilated sebaceous glands filled with sebaceous and keratinized material. Surrounding the gland is a slight infiltration of lymphocytes. In the early cyst the sebaceous gland is enlarged with abscess formation. In the center of this is a large plug made up of sebaceous and keratinoid material Around the gland is an exudate made up of polymorphonuclear leukocytes In these earlier lesions no giant cells are noted. In the late lesions however multinucleated giant cells are found. The epidermis shows some acanthosis.

PROGNOSIS

While these patients remain in the tropics their condition becomes steadily worse More and more lesions develop and the areas of involvement become more extensive With the spread of the eruption there is an increase in the amount of discomfort and pain so that the patient has difficulty in carrying on.

Patients returning to a cooler climate usually notice improvement but the deeper lesions will continue to drain and be active for many months There is little if any improvement in the keloidal scars With our present knowledge it is impossible to predict who is likely to acquire tropical acne on going to hot climates.

THERAPY

The usual therapeutic procedures for acne vulgaris are not effective when used in the tropics. When patients with this disease return to cooler climates they respond to orthodox methods of treatment but their response is usually very slow

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ADDENDA ET CORRIGENDA

Page 50 Fig 33 add to caption of Fig. 33 "Although moniliasis of the intestines as a pure aetiological entity is still problematic, candida most probably only growing luxuriantly in sufferers from malnutrition, diabetes, cachexia, etc., the *ecological balance* (*i.e.* the relation of organisms to each other) of the intestinal flora can be changed, even fatally by means of antibiotics. The latter eliminate an important part of the bacterial flora. The yeast like organisms may expand in this "vacuum" without a natural check, eventually causing fatal moniliasis (APPENDIX Vol. II).

Page 59 Fig. 44 It has been said, in the caption of Fig. 44 that a universal diffusion of cheiropompholyx is called tropical cheiropompholyx. Since, however *cheir* means *hand* one should of course speak of tropical pompholyx, as has also been stated in the text of page 59.

Page 80 Fig. 71 By some unfortunate mistake the name of Dr Pinkus-Monroe (Mich) has been omitted as the contributor of this photograph.

Page 194 3rd line, The figure indicated should be 188

Page 195 2nd line, underneath picture the figure indicated should be 143.